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=> FILE HOME
FILE 'HOME' ENTERED AT 11:35:55 ON 29 AUG 2008


=> DISPLAY HISTORY FULL L1-

     FILE 'HCA, WPIX, JAPIO' ENTERED AT 10:51:03 ON 29 AUG 2008
L1           542 SEA ROTAR?(3A)(PRESS OR PRESSES OR PRESSED OR PRESSING#)
L2          5563 SEA ROTAR?(3A)(PRESS OR PRESSES OR PRESSED OR PRESSING#)
L3          4473 SEA ROTAR?(3A)(PRESS OR PRESSES OR PRESSED OR PRESSING#)
     TOTAL FOR ALL FILES
L4         10578 SEA ROTAR?(3A)(PRESS OR PRESSES OR PRESSED OR PRESSING#)
L5        150513 SEA TABLET? OR CAPLET? OR CAPSULE? OR LOZENGE?
L6         99778 SEA TABLET? OR CAPLET? OR CAPSULE? OR LOZENGE?
L7         22475 SEA TABLET? OR CAPLET? OR CAPSULE? OR LOZENGE?
     TOTAL FOR ALL FILES
L8        272766 SEA TABLET? OR CAPLET? OR CAPSULE? OR LOZENGE?
L9        109429 SEA (AIR# OR ATM# OR ATMOS?)(2A)(PURIF? OR CIRCULAT? OR
                 CONTROL? OR REGULAT? OR GOVERN? OR FILT?)
L10       146391 SEA (AIR# OR ATM# OR ATMOS?)(2A)(PURIF? OR CIRCULAT? OR
                 CONTROL? OR REGULAT? OR GOVERN? OR FILT?)
L11        59482 SEA (AIR# OR ATM# OR ATMOS?)(2A)(PURIF? OR CIRCULAT? OR
                 CONTROL? OR REGULAT? OR GOVERN? OR FILT?)
     TOTAL FOR ALL FILES
L12       315302 SEA (AIR# OR ATM# OR ATMOS?)(2A)(PURIF? OR CIRCULAT? OR
                 CONTROL? OR REGULAT? OR GOVERN? OR FILT?)
L13       725843 SEA CLIMATE? OR ENVIRONMENT?
L14       325542 SEA CLIMATE? OR ENVIRONMENT?
L15       115438 SEA CLIMATE? OR ENVIRONMENT?
     TOTAL FOR ALL FILES
L16      1166823 SEA CLIMATE? OR ENVIRONMENT?
L17      3622913 SEA TEMP# OR TEMPERATURE#
L18      1444235 SEA TEMP# OR TEMPERATURE#
L19       726326 SEA TEMP# OR TEMPERATURE#
     TOTAL FOR ALL FILES
L20      5793474 SEA TEMP# OR TEMPERATURE#
L21       304262 SEA HUMID? OR MOISTUR?
L22       262243 SEA HUMID? OR MOISTUR?
L23       113356 SEA HUMID? OR MOISTUR?
     TOTAL FOR ALL FILES
L24       679861 SEA HUMID? OR MOISTUR?
L25       406002 SEA (INJECT? OR INTRODUC? OR APPLY? OR APPLIED OR
                 APPLICATION? OR SUPPLY? OR SUPPLIED OR SUPPLICATION? OR
                 FURNISH? OR TREAT? OR PRETREAT? OR CONDITION? OR
                 PRECONDITION? OR PROCESS? OR PORT# OR PORTAL? OR STREAM?
                 OR FLOW OR FLOWS OR FLOWED OR FLOWING#)(2A)(GAS## OR
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                GASEOUS? OR GASIF? OR AIR#)
L26       650779 SEA (INJECT? OR INTRODUC? OR APPLY? OR APPLIED OR
                APPLICATION? OR SUPPLY? OR SUPPLIED OR SUPPLICATION? OR
                FURNISH? OR TREAT? OR PRETREAT? OR CONDITION? OR
                PRECONDITION? OR PROCESS? OR PORT# OR PORTAL? OR STREAM?
                OR FLOW OR FLOWS OR FLOWED OR FLOWING#)(2A)(GAS## OR
                GASEOUS? OR GASIF? OR AIR#)
L27       329987 SEA (INJECT? OR INTRODUC? OR APPLY? OR APPLIED OR
                APPLICATION? OR SUPPLY? OR SUPPLIED OR SUPPLICATION? OR
                FURNISH? OR TREAT? OR PRETREAT? OR CONDITION? OR
                PRECONDITION? OR PROCESS? OR PORT# OR PORTAL? OR STREAM?
                OR FLOW OR FLOWS OR FLOWED OR FLOWING#)(2A)(GAS## OR
                GASEOUS? OR GASIF? OR AIR#)
     TOTAL FOR ALL FILES
L28      1386768 SEA (INJECT? OR INTRODUC? OR APPLY? OR APPLIED OR
                APPLICATION? OR SUPPLY? OR SUPPLIED OR SUPPLICATION? OR
                FURNISH? OR TREAT? OR PRETREAT? OR CONDITION? OR
                PRECONDITION? OR PROCESS? OR PORT# OR PORTAL? OR STREAM?
                OR FLOW OR FLOWS OR FLOWED OR FLOWING#)(2A)(GAS## OR
                GASEOUS? OR GASIF? OR AIR#)
L29           132 SEA L1 AND L5
L30           267 SEA L2 AND L6
L31            13 SEA L3 AND L7
     TOTAL FOR ALL FILES
L32           412 SEA L4 AND L8
L33             0 SEA L29 AND L9
L34             0 SEA L30 AND L10
L35             0 SEA L31 AND L11
     TOTAL FOR ALL FILES
L36             0 SEA L32 AND L12
L37             1 SEA L29 AND L13
L38            19 SEA L30 AND L14
L39             0 SEA L31 AND L15
     TOTAL FOR ALL FILES
L40            20 SEA L32 AND L16
L41            13 SEA L29 AND L17
L42            39 SEA L30 AND L18
L43             0 SEA L31 AND L19
     TOTAL FOR ALL FILES
L44            52 SEA L32 AND L20
L45            14 SEA L29 AND L21
L46            33 SEA L30 AND L22
L47             0 SEA L31 AND L23
     TOTAL FOR ALL FILES
L48            47 SEA L32 AND L24
L49             4 SEA L41 AND L45
L50            12 SEA L42 AND L46
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L51           0 SEA L43 AND L47
     TOTAL FOR ALL FILES
L52          16 SEA L44 AND L48
L53           2 SEA L29 AND L25
L54          12 SEA L30 AND L26
L55           0 SEA L31 AND L27
     TOTAL FOR ALL FILES
L56          14 SEA L32 AND L28
L57        9836 SEA PILL OR PILLS
L58       11906 SEA PILL OR PILLS
L59         655 SEA PILL OR PILLS
     TOTAL FOR ALL FILES
L60       22397 SEA PILL OR PILLS
L61           1 SEA L1 AND L57
L62           5 SEA L2 AND L58
L63           0 SEA L3 AND L59
     TOTAL FOR ALL FILES
L64           6 SEA L4 AND L60
L65           1 SEA L61 AND (L9 OR L13 OR L17 OR L21 OR L25)
L66           0 SEA L62 AND (L10 OR L14 OR L18 OR L22 OR L26)
L67           0 SEA L63 AND (L11 OR L15 OR L19 OR L23 OR L27)
     TOTAL FOR ALL FILES
L68           1 SEA L64 AND (L12 OR L16 OR L20 OR L24 OR L28)
L69       44066 SEA AIR#(2A)CONDITION? OR CIRCULAT?(2A)SYSTEM?
L70      144977 SEA AIR#(2A)CONDITION? OR CIRCULAT?(2A)SYSTEM?
L71       74913 SEA AIR#(2A)CONDITION? OR CIRCULAT?(2A)SYSTEM?
     TOTAL FOR ALL FILES
L72      263956 SEA AIR#(2A) CONDITION? OR CIRCULAT?(2A) SYSTEM?
L73      484181 SEA EVACUAT? OR VACUUM? OR INVACUO# OR VACUO#
L74      362517 SEA EVACUAT? OR VACUUM? OR INVACUO# OR VACUO#
L75      149893 SEA EVACUAT? OR VACUUM? OR INVACUO# OR VACUO#
     TOTAL FOR ALL FILES
L76      996591 SEA EVACUAT? OR VACUUM? OR INVACUO# OR VACUO#
L77           0 SEA L61 AND L69
L78           0 SEA L62 AND L70
L79           0 SEA L63 AND L71
     TOTAL FOR ALL FILES
L80           0 SEA L64 AND L72
L81           0 SEA L61 AND L73
L82           0 SEA L62 AND L74
L83           0 SEA L63 AND L75
     TOTAL FOR ALL FILES
L84           0 SEA L64 AND L76
L85           1 SEA L29 AND L69
L86           1 SEA L30 AND L70
L87           0 SEA L31 AND L71
     TOTAL FOR ALL FILES
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L88           2 SEA L32 AND L72
L89           0 SEA L29 AND L73
L90          11 SEA L30 AND L74
L91           0 SEA L31 AND L75
     TOTAL FOR ALL FILES
L92          11 SEA L32 AND L76

     FILE 'HCAPLUS' ENTERED AT 11:06:02 ON 29 AUG 2008
L93         285 SEA BRISSET ?/AU
L94           5 SEA BATTUNG ?/AU
L95           1 SEA L93 AND L94

     FILE 'LCA' ENTERED AT 11:11:01 ON 29 AUG 2008
L96          50 SEA (PRODUC? OR PROD# OR GENERAT? OR MANUF? OR MFR# OR
                CREAT? OR FORM## OR FORMING# OR FORMAT? OR MAKE# OR
                MADE# OR MAKING# OR FABRICAT? OR SYNTHESI? OR PREPAR? OR
                PREP#)(2A)(TABLET? OR CAPLET? OR CAPSULE# OR PILL OR
                PILLS OR LOZENG?)
L97        2148 SEA (DRUG? OR MEDICINE? OR NOSTRUM? OR MEDICAMENT? OR
                PALLIATIV? OR ALLEVIATIV? OR LENITIV? OR ASSUASIV? OR
                PROPHYLACT? OR ANALGESIC? OR ANESTHETIC? OR ANTISEPTIC?
                OR ANTIBIOTIC?)/BI,AB
L98          41 SEA ((THERAPEUTIC? OR CURATIV? OR REMEDIAL? OR PHARMAC?)(
                A)(AGENT? OR COMPOUND# OR CPD# OR COMP# OR COMPSN# OR
                COMPOSIT?))/BI,AB
L99        1123 SEA PHARMACOLOG? OR PHARMAC? OR MEDICINAL?

     FILE 'HCA, WPIX, JAPIO' ENTERED AT 11:14:55 ON 29 AUG 2008
L100      30502 SEA L96 AND (L97 OR L98 OR L99)
L101      18986 SEA L96 AND (L97 OR L98 OR L99)
L102        965 SEA L96 AND (L97 OR L98 OR L99)
     TOTAL FOR ALL FILES
L103      50453 SEA L96 AND (L97 OR L98 OR L99)
L104         70 SEA L100 AND L1
L105         82 SEA L101 AND L2
L106          0 SEA L102 AND L3
     TOTAL FOR ALL FILES
L107        152 SEA L103 AND L4
L108         16 SEA L104 AND (L9 OR L13 OR L17 OR L21 OR L25 OR L69 OR
                L73)
L109         36 SEA L105 AND (L10 OR L14 OR L18 OR L22 OR L26 OR L70 OR
                L74)
L110          0 SEA L106 AND (L11 OR L15 OR L19 OR L23 OR L27 OR L71 OR
                L75)
     TOTAL FOR ALL FILES
L111         52 SEA L107 AND (L12 OR L16 OR L20 OR L24 OR L28 OR L72 OR
                L76)
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L112     290242 SEA PRESS OR PRESSES OR PRESSED OR PRESSING#
L113     620052 SEA PRESS OR PRESSES OR PRESSED OR PRESSING#
L114     381421 SEA PRESS OR PRESSES OR PRESSED OR PRESSING#
     TOTAL FOR ALL FILES
L115     663174 SEA PRESS OR PRESSES OR PRESSED OR PRESSING# OR MOULD?
                OR MOLD?
L116    1246598 SEA PRESS OR PRESSES OR PRESSED OR PRESSING# OR MOULD?
                OR MOLD?
L117     716930 SEA PRESS OR PRESSES OR PRESSED OR PRESSING# OR MOULD?
                OR MOLD?
     TOTAL FOR ALL FILES
L118    2626702 SEA PRESS OR PRESSES OR PRESSED OR PRESSING# OR MOULD?
                OR MOLD?
L119       1197 SEA L100 AND L115
L120       1598 SEA L101 AND L116
L121         74 SEA L102 AND L117
     TOTAL FOR ALL FILES
L122       2869 SEA L103 AND L118
L123          5 SEA L119 AND L9
L124          9 SEA L120 AND L10
L125          0 SEA L121 AND L11
     TOTAL FOR ALL FILES
L126         14 SEA L122 AND L12
L127         17 SEA L119 AND L13
L128         74 SEA L120 AND L14
L129          0 SEA L121 AND L15
     TOTAL FOR ALL FILES
L130         91 SEA L122 AND L16
L131        139 SEA L119 AND L17
L132        314 SEA L120 AND L18
L133          2 SEA L121 AND L19
     TOTAL FOR ALL FILES
L134        455 SEA L122 AND L20
L135          2 SEA L131 AND L127
L136         24 SEA L132 AND L128
L137          0 SEA L133 AND L129
     TOTAL FOR ALL FILES
L138         26 SEA L134 AND L130
L139         93 SEA L119 AND L21
L140        204 SEA L120 AND L22
L141          2 SEA L121 AND L23
     TOTAL FOR ALL FILES
L142        299 SEA L122 AND L24
L143         13 SEA L119 AND L25
L144         43 SEA L120 AND L26
L145          1 SEA L121 AND L27
     TOTAL FOR ALL FILES
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L146         57 SEA L122 AND L28
L147          5 SEA L119 AND L69
L148          9 SEA L120 AND L70
L149          0 SEA L121 AND L71
     TOTAL FOR ALL FILES
L150         14 SEA L122 AND L72
L151         56 SEA L119 AND L73
L152         86 SEA L120 AND L74
L153          2 SEA L121 AND L75
     TOTAL FOR ALL FILES
L154        144 SEA L122 AND L76
L155          5 SEA L139 AND L143
L156         10 SEA L140 AND L144
L157          0 SEA L141 AND L145
     TOTAL FOR ALL FILES
L158         15 SEA L142 AND L146
L159          6 SEA L139 AND L151
L160         15 SEA L140 AND L152
L161          1 SEA L141 AND L153
     TOTAL FOR ALL FILES
L162         22 SEA L142 AND L154
L163          0 SEA L143 AND L151
L164          8 SEA L144 AND L152
L165          0 SEA L145 AND L153
     TOTAL FOR ALL FILES
L166          8 SEA L146 AND L154

     FILE 'HCA' ENTERED AT 11:26:50 ON 29 AUG 2008
L167         25 SEA L37 OR L49 OR L53 OR L65 OR L85 OR L123 OR L135 OR
                L147 OR L155 OR L159
L168         12 SEA L108 NOT L167

     FILE 'WPIX' ENTERED AT 11:28:45 ON 29 AUG 2008
L169         30 SEA L86 OR L124 OR L148 OR L156 OR L164
L170         58 SEA (L38 OR L50 OR L54 OR L90 OR L160) NOT L169
L171         40 SEA (L109 OR L136) NOT (L169 OR L170)
L172         22 SEA 1840-2003/PY,PRY,AY AND L169
L173         41 SEA 1840-2003/PY,PRY,AY AND L170
L174         28 SEA 1840-2003/PY,PRY,AY AND L171

     FILE 'HCA' ENTERED AT 11:32:26 ON 29 AUG 2008
L175         19 SEA 1840-2003/PY,PRY,AY AND L167
L176         12 SEA 1840-2003/PY,PRY,AY AND L168
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=> FILE HCA
FILE 'HCA' ENTERED AT 11:36:12 ON 29 AUG 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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=> D L175 1-19 BIB ABS HITIND

L175 ANSWER 1 OF 19  HCA  COPYRIGHT 2008 ACS on STN
AN   144:177408  HCA  Full-text
TI   Helicid soft capsule
IN   Zhao, Yong
PA   Kunming Zijian Biotechnology Co., Ltd., Peop. Rep. China
SO   Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp.
     CODEN: CNXXEV
DT   Patent
LA   Chinese
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------
     --------
PI   CN 1596903           A     20050323    CN 2003-135874
                                                                  200309
                                                                  20
                                                 <--
PRAI CN 2003-135874              20030920  <--
AB   The helicid soft capsule is comprised of liq. medicine that contains
     >200 μm helicid 50-200 mg, and addnl. pharmaceutic or edible
     adjuvant.  The pharmaceutic or edible adjuvant is one or more of
     refined rice oil, safflower oil, linseed oil, α-linseed oil, γ-
     linseed oil, etc.  The liq. medicine or capsule also contains one or
     more of carthamin yellow, amaranth, brilliant black, etc., and one or
     more of lemon essence, orange essence, vanillin, menthol, ketone
     musk, etc.  The helicid is prepd. by superfine treating helicid into
     200 μm particles, adding the superfine helicid to the matrix of
     solvent, stirring, homogenizing, emulsifying, filtering, degassing,
     placing in the kettle above the filling machine; dissolving capsule
     material, conserving temp. at 40-50°; pressing pills with rotary
     block press at 10000 degree and 21-25°, and RH% = 39-41%, prepg. the
     soft capsule, cleaning, drying at 28±2° for 19-27 h, and subpackaging
     to obtain the product.
IC   ICM  A61K031-7048
     ICS  A61K009-48; A61P025-20
CC   63-4 (Pharmaceuticals)
```

L175 ANSWER 2 OF 19 HCA COPYRIGHT 2008 ACS on STN
AN 140:117397 HCA Full-text
TI Drugs containing vardenafil hydrochloride trihydrate prepared by rehydration
IN Serno, Peter; Grunenberg, Alfons; Ohm, Andreas; Bellinghausen, Rainer; Vollers, Eimer; Henck, Jan-Olav
PA Bayer Healthcare AG, Germany
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004006894	A1	20040122	WO 2003-EP7093	200307 03
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10232113	A1	20040129	DE 2002-10232113	200207 16
			<--	
CA 2492747	A1	20040122	CA 2003-2492747	200307 03
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AU 2003249942	A1	20040202	AU 2003-249942	200307 03
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BR 2003005559	A	20040928	BR 2003-5559	200307 03
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EP 1523303 A1 20050420 EP 2003-763695
200307
03
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CN 1681481 A 20051012 CN 2003-821144
200307
03
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JP 2005533836 T 20051110 JP 2004-520469
200307
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NZ 537698 A 20061027 NZ 2003-537698
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MX 2005PA00554 A 20050428 MX 2005-PA554
200501
12
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NO 2005000578 A 20050202 NO 2005-578
200502
02
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US 20060111354 A1 20060525 US 2005-521534
200508
31
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ZA 2005000268 A 20060329 ZA 2005-268
200601
12
<--
IN 2007DN03185 A 20070831 IN 2007-DN3185
200704
27
<--
PRAI DE 2002-10232113 A 20020716 <--
WO 2003-EP7093 W 20030703 <--
IN 2005-DN103 A3 20050112
AB The invention relates to a method for producing medicaments that contain vardenafil hydrochloride, essentially as trihydrate in solid form, and to medicaments that can be obtained according to this method. Tablets and coated tablets are prepd. from compns. that contain vardenafil hydrochloride with undefined water content; these

tablets are contacted with humid air until vardenafil hydrochloride trihydrate is formed. Thus coated tablets were prepd. by mixing 216 g microfine vardenafil HCl, 605 g microcryst. cellulose and 43.2 g Crospovidine, followed by the addn. of 2101 g cellulose and 132 g Crospovidine; thereafter 350 g cellulose, 17.5 g highly dispersed silica and 35 g magnesium stearate were dosed. Tablets with 6 mm diam. and 87 mg wt. were pressed; they contained 5 mg vardenafil base. Tablets were coated (43.5 mg/tablet) with a suspension that included (%): hypromellose 4.5; Macrogol 400 1.5; titanium dioxide 1.23; iron oxide yellow 0.25; iron oxide red 0.02. The tablets were rehydrated in a fluidized bed granulator for 4 h at 150 m3/h air flow at 30°C and 19 g/kg water content (corresponds to 70% relative humidity). The product contains vardenafil hydrochloride trihydrate; the dissoln. takes place in 0.5 min compared to the non-rehydrated tablets with 2 min of dissoln.

IC ICM A61K009-28
ICS A61K031-53; A61P015-10
CC 63-6 (Pharmaceuticals)
IT Dissolution
(drugs contg. vardenafil hydrochloride trihydrate prepd. by rehydration)
IT Air
(humid; drugs contg. vardenafil hydrochloride trihydrate prepd. by rehydration)
IT Sexual disorders
(impotence; drugs contg. vardenafil hydrochloride trihydrate prepd. by rehydration)
IT Hydration, chemical
(rehydration; drugs contg. vardenafil hydrochloride trihydrate prepd. by rehydration)
IT Humidity
(relative; drugs contg. vardenafil hydrochloride trihydrate prepd. by rehydration)
IT Drug delivery systems
(tablets, coated; drugs contg. vardenafil hydrochloride trihydrate prepd. by rehydration)
IT Drug delivery systems
(tablets; drugs contg. vardenafil hydrochloride trihydrate prepd. by rehydration)
IT 224785-91-5, Vardenafil hydrochloride 330808-88-3
(drugs contg. vardenafil hydrochloride trihydrate prepd. by rehydration)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L175 ANSWER 3 OF 19 HCA COPYRIGHT 2008 ACS on STN
AN 139:399607 HCA Full-text

TI Enalapril maleate form II: stabilization in a tablet formulation
AU Eyjolfsson, R.
CS Drug Development, Hafnarfjordur, Iceland
SO Pharmazie (2003), 58(5), 357
CODEN: PHARAT; ISSN: 0031-7144
PB Govi-Verlag Pharmazeutischer Verlag GmbH
DT Journal
LA English
AB Two polymorphic forms, form I and form II, of enalapril maleate have been described and characterized by spectroscopic methods. Form II is thermodynamically more stable than form I but the energy difference between these two polymorphs has been stated to be very small or only 0.6 kcal/mol. However, evidence has been presented suggesting that form II is much more unstable than form I in a tablet formulation contg. sodium hydrogen carbonate as stabilizer in a practically stoichiometric amt. The enalapril maleate used in this study was practically pure form II as ascertained by x-ray powder diffraction anal. Batch size was 5.2 kg, main excipient lactose monohydrate, tablet strength 10 mg, tablet mass 130 mg, wet granulation, drying of granulate to 1.4 % (1.3-1.5%) loss on drying (IR-balance, 105°), compaction in a rotary tablet press. All processing steps, including packaging were performed at ambient (room) temp. and humidity (approx. 65 % RH). The tablets obtained were packaged into Al/Al blisters and high d. polyethylene containers with desiccant (HDPE + Des) and put on stability trial at 40°/75 % RH for one month. Batch 1 contained sodium hydrogen carbonate in a practically stoichiometric quantity (5 mg per tablet) to enalapril maleate (10 mg per tablet), the percentages shown for the other batches are relative to this amt. These results demonstrate a dramatic decrease in DKP-content with increasing amts. of sodium hydrogen carbonate. On the other hand its effects on the content of enalaprilate seem to be marginal or nonexistent. The formation of this degradate (arising from hydrolysis of the Et ester vector in the drug mol.) probably reflects residual (free) moisture in the tablets. This assumption is substantiated by the fact that significantly less degrdn. takes place on storage in the presence of desiccant.
CC 63-6 (Pharmaceuticals)
ST enalapril maleate tablet stability
IT Polymorphism (crystal)
Stability
(enalapril maleate form II and stabilization in tablet formulation)
IT Drug delivery systems
(tablets; enalapril maleate form II and stabilization in tablet formulation)
IT 106-57-0, Diketopiperazine

(enalapril maleate form II and stabilization in tablet formulation)
IT 76095-16-4, Enalapril maleate
(enalapril maleate form II and stabilization in tablet formulation)
IT 144-55-8, Sodium bicarbonate, biological studies
(enalapril maleate form II and stabilization in tablet formulation)
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L175 ANSWER 4 OF 19 HCA COPYRIGHT 2008 ACS on STN
AN 136:330445 HCA Full-text
TI Polymorphic changes of thiamine hydrochloride during granulation and tableting
AU Wostheinrich, K.; Schmidt, P. C.
CS Department of Pharmaceutical Technology, University of Tubingen, Tubingen, D-72076, Germany
SO Drug Development and Industrial Pharmacy (2001), 27(6), 481-489
CODEN: DDIPD8; ISSN: 0363-9045
PB Marcel Dekker, Inc.
DT Journal
LA English
AB Thiamine-HCl (I) was granulated by using an instrumented fluidized bed granulator (Huttlin HKC 05-TJ). Granules consisting of pure I were produced using an aq. soln. of I as the granulating liq. The effects of process variables such as inlet air temp., spray rate, and amt. of granulating liq. on granule properties are described. Particle size distributions of granules depended mainly on the amt. of granulating liq. sprayed into the powder bed. Granules were tableted on a rotary tablet press at 4 different compression forces. Crushing strengths and disintegration times of all tablets were very low after manuf., but increased considerably after 4 mo of storage at room temp. Granular materials showed "caking" under the same storage conditions. These changes could be attributed to alterations of the polymorphic form of I. The water-free form, being present directly after granulation, absorbs humidity very fast and is transformed into the monohydrate, which is stable at room temp. Loss of water takes place during the drying phase of the granulation process and on storage of the substance at 50 and 80°. During storage at room temp. while exposed to humidity, a transformation into the hemihydrate was obsd. This polymorph is transformed during thermal anal. at about 190° to a water-free form that is stable at higher temps.
CC 63-5 (Pharmaceuticals)
ST thiamine polymorph granulation tablet
IT Granulation

(fluidized-bed; polymorphic changes of thiamine during granulation and tableting)

IT Drug delivery systems
(granules; polymorphic changes of thiamine during granulation and tableting)

IT Compression
Crushing strength
Granulation
Humidity
Particle size distribution
Polymorphism (crystal)
Storage
(polymorphic changes of thiamine during granulation and tableting)

IT Drug delivery systems
(tablets; polymorphic changes of thiamine during granulation and tableting)

IT 67-03-8, Thiamine hydrochloride 6779-97-1, Thiamine hydrochloride monohydrate 415706-86-4
(polymorphic changes of thiamine during granulation and tableting)

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L175 ANSWER 5 OF 19 HCA COPYRIGHT 2008 ACS on STN

AN 133:125173 HCA Full-text

TI Evaluation and validation of a fully instrumented Huttlin HKC 05-TJ laboratory-scale fluidized bed granulator

AU Wostheinrich, K.; Schmidt, P. C.

CS Department of Pharmaceutical Technology, University of Tubingen, Tubingen, D-72076, Germany

SO Drug Development and Industrial Pharmacy (2000), 26(6), 621-633
CODEN: DDIPD8; ISSN: 0363-9045

PB Marcel Dekker, Inc.

DT Journal

LA English

AB The instrumentation and validation of a lab.-scale fluidized bed app. is described. For continuous control of the process, the app. is instrumented with sensors for temp., relative humidity (RH), and air velocity. Conditions of inlet air, fluidizing air, product, and exhaust air were detd. The temp. sensors were calibrated at temps . of 0.0°C and 99.9°C. The calibration of the humidity sensors covered the range from 12% RH to 98% RH using satd. electrolyte solns. The calibration of the anemometer took place in a wind tunnel at defined air velocities. The calibrations led to satisfying results concerning sensitivity and precision. To evaluate the

reproducibility of the process, 15 granules were prepd. under identical conditions. The influence of the type of pump used for delivering the granulating liq. was investigated. Particle size distribution, bulk d., and tapped d. were detd. Granules were tableted on a rotary press at four different compression force levels, followed by detn. of tablet properties such as wt., crushing strength, and disintegration time. The app. was found to produce granules with good reproducibility concerning the granule and tablet properties.

CC 63-6 (Pharmaceuticals)

ST fluidized bed granulator tablet

IT Drug delivery systems
(tablets; evaluation and validation of a fully instrumented Huttlin HKC 05-TJ lab.-scale fluidized bed granulator)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L175 ANSWER 6 OF 19 HCA COPYRIGHT 2008 ACS on STN

AN 133:22442 HCA Full-text

TI Pharmaceutical combination preparations for treatment of cardiac and cardiovascular disorders

IN Heller, Rudolf

PA F. Hoffmann-La Roche A.-G., Switz.

SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000032174	A2	20000608	WO 1999-EP8972	19991120
			<--	
WO 2000032174	A3	20001116		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2352361	A1	20000608	CA 1999-2352361	19991

20
<--
CA 2352361 C 20070102
BR 9915610 A 20010814 BR 1999-15610
199911
20
<--
EP 1131072 A2 20010912 EP 1999-957320
199911
20
<--
EP 1131072 B1 20030423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
TR 200101470 T2 20011121 TR 2001-1470
199911
20
<--
TR 200200981 T2 20020621 TR 2002-981
199911
20
<--
TR 200200982 T2 20020621 TR 2002-982
199911
20
<--
JP 2002531395 T 20020924 JP 2000-584870
199911
20
<--
AT 238056 T 20030515 AT 1999-957320
199911
20
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PT 1131072 T 20030829 PT 1999-957320
199911
20
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AU 765977 B2 20031009 AU 2000-15065
199911
20
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ES 2195638 T3 20031201 ES 1999-957320
199911
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US 6403579 B1 20020611 US 1999-447872

				199911 23
			<--	
TW 228414	B	20050301	TW 2000-89103144	
				200002 23
			<--	
ZA 2001004280	A	20020826	ZA 2001-4280	
				200105 24
			<--	
MX 2001PA05300	A	20010910	MX 2001-PA5300	
				200105 25
			<--	
US 20020052367	A1	20020502	US 2001-946205	
				200109 05
			<--	
US 20040087578	A1	20040506	US 2003-693243	
				200310 24
			<--	
JP 2007077160	A	20070329	JP 2006-284476	
				200610 19
			<--	

PRAI	EP 1998-122489	A	19981127	<--
	JP 2000-584870	A3	19991120	<--
	WO 1999-EP8972	W	19991120	<--
	US 1999-447872	A3	19991123	<--
	US 2001-946205	B1	20010905	<--

AB Pharmaceutical prepns. for the treatment of cardiac and cardiovascular disorders such as hypertension, angina pectoris, cardiac insufficiency, and illnesses assocd. therewith contain carvedilol, a β-blocker with addnl. α1-blocking activity, or a salt thereof and hydrochlorothiazide, a diuretic, or a salt thereof as a fixed combination of active substances, as well as usual additives. The process for prodn. of the combination prepn. permits the 2 active substance granulates to be pressed to a stable tablet in 1 operation, as follows: granulates of the 2 agents, each having a moisture content of 6-20% and a bulk d. of 0.1-1.5 g/mL, and the granulate moisture content and bulk d. of the 2 granulates differing from one another by ≤30%. are combined to a press mass which is compressed to a solid dosage form, preferably a tablet. Since carvedilol is light sensitive, the dosage form is coated with a light-protecting film. At disintegrant contents >5%, the coating is applied at an initial

spray rate sufficiently low to permit formation of a film on the tablet surface under conditions of air supply and temp. which remove the water of the film suspension as rapidly as possible from the tablet surface; after this crit. phase of film formation is complete, the spray rate is increased to that conventional for film-coating. Thus, tablets were prepd. contg. carvedilol 25.000, hydrochlorothiazide 12.500, sucrose 25.000, lactose-H2O 28.060, PVP 1.780, crosslinked PVP 20.170, microcryst. cellulose 10.000, highly dispersed SiO2 5.320, and Mg stearate 2.170 mg, and coated with a mixt. of Et acrylate/Me acrylate copolymer 2.248, Na citrate 0.308, hydroxypropylmethylcellulose 1.018, Macrogol 0.644, talc 1.624, TiO2 0.950, indigo carmine color lacquer 0.170, polysorbate 80 0.034, and dimethicone 0.004 mg.

IC ICM A61K031-00

CC 63-6 (Pharmaceuticals)

IT Heart, disease
(failure; pharmaceutical combination prepns. for treatment of cardiac and cardiovascular disorders)

IT Antianginal agents
Antihypertensives
Cardiovascular agents
Coating process
Heart, disease
(pharmaceutical combination prepns. for treatment of cardiac and cardiovascular disorders)

IT Drug delivery systems
(solids; pharmaceutical combination prepns. for treatment of cardiac and cardiovascular disorders)

IT Drug delivery systems
(tablets, coated; pharmaceutical combination prepns. for treatment of cardiac and cardiovascular disorders)

IT 58-93-5, Hydrochlorothiazide 72956-09-3, Carvedilol
(pharmaceutical combination prepns. for treatment of cardiac and cardiovascular disorders)

L175 ANSWER 7 OF 19 HCA COPYRIGHT 2008 ACS on STN

AN 131:291305 HCA Full-text

TI Starch capsules containing microorganisms and/or polypeptides or proteins

IN Myllarinen, Paivi; Forssell, Pirkko; Von Wright, Atte; Alander, Minna; Mattila-Sandholm, Tiina; Poutanen, Kaisa

PA Valtion Teknillinen Tutkimuskeskus, Finland

SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9952511	A1	19991021	WO 1999-FI259	199903 29
				<--	
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FI 9800707	A	19990928	FI 1998-707	199803 27
				<--	
	FI 104405	B1	20000131		
	CA 2324364	A1	19991021	CA 1999-2324364	199903 29
				<--	
	AU 9930386	A	19991101	AU 1999-30386	199903 29
				<--	
	BR 9909133	A	20001205	BR 1999-9133	199903 29
				<--	
	EP 1063976	A1	20010103	EP 1999-911844	199903 29
				<--	
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
	JP 2002511403	T	20020416	JP 2000-543121	199903 29
				<--	
PRAI	FI 1998-707	A	19980327	<--	
	WO 1999-FI259	W	19990329	<--	

AB The invention relates to starch capsules which protect various substances, such as living microbes or enzymes, against the effect of the environment or the intestines, and to a method for manufg. such

capsules. A fraction of a suitable size category is chosen from the starch granules, the porosity of the granules is improved by hydrolyzing, and the granules are filled with desired substances, such as living microbes and/or enzymes. When desired, the starch granules can be coated with a suitable biopolymer, such as starch or amylose. A 10% suspension of large starch granules (30-100 μm) (prepn. given) was added to α-amylase (1000-10,000 U/g of granules). Hydrolysis was allowed to take place overnight at a temp of over 30°. The soln. was then centrifuged and the sediment was freeze-dried. Then, 10 g starch granules and 100 mL of a soln. of Lactobacillus rhamnosus (108-109 CFU/mL) was mixed and stirred at 30° over night. The soln. was then centrifuged, washed with water, and freeze-dried. The no. of the bacteria after 2 mo storage at 20° as 3x105 CFU/g.

IC ICM A61K009-52
ICS A61K009-20; A61K047-36

CC 63-6 (Pharmaceuticals)

IT Drug delivery systems
(granules; starch capsules contg. microorganisms and/or polypeptides or proteins)

IT Bacteria (Eubacteria)
Bifidobacterium
Corynebacterium
Enterococcus
Lactobacillus
Lactobacillus rhamnosus
Lactococcus
Lactococcus lactis
Leuconostoc
Microorganism
Mold (fungus)
Particle size
Pediococcus
Saccharomyces
Streptococcus
Yeast
(starch capsules contg. microorganisms and/or polypeptides or proteins)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L175 ANSWER 8 OF 19 HCA COPYRIGHT 2008 ACS on STN
AN 129:100022 HCA Full-text
OREF 129:20495a,20498a
TI Procedure and device for monitoring parameters of tablets
IN Fiedler, Juergen; Hegel, Walter; Bargenda, Hagen; Koerner, Hans Georg; Wagner, Udo; Stepanek, Josef
PA Korsch Pressen G.m.b.H., Germany

SO Ger. Offen., 10 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19654612	A1	19980702	DE 1996-19654612	19961220 <--
	DE 19654612	C2	19990701		
	JP 10253617	A	19980925	JP 1997-365284	19971219 <--

PRAI DE 1996-19654612 A 19961220 <--

AB An automated device for monitoring the wt., height, and/or hardness of tablets produced by a rotary tablet press comprises a sample container which dispenses single tablets to anal. stations for detn. of these parameters, or dispenses multiple tablets for detn. of tablet wt. The sample container has slanted inner surfaces and is divided longitudinally for opening at the bottom to dispense tablets. Single tablets are manipulated with a suction arm ending in a slightly convex sieve head which lifts the tablet by air flow.

IC ICM G01N033-15
ICS G01G013-00; G01G019-414; G01B021-08; G01N003-40; G01N005-00; A61J003-10; B30B011-08; B30B015-00
ICA B65G051-02
CC 63-5 (Pharmaceuticals)
ST tablet phys property detn app; hardness detn
tablet app
IT Apparatus
Dispensing apparatus
(automated; procedure and device for monitoring parameters of tablets)
IT Balances
Hardness (mechanical)
Weighing
(procedure and device for monitoring parameters of tablets)
IT Drug delivery systems
(tablets; procedure and device for monitoring parameters of tablets)
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L175 ANSWER 9 OF 19 HCA COPYRIGHT 2008 ACS on STN
AN 122:196753 HCA Full-text
OREF 122:35793a,35796a
TI Morphological, packing, flow and tableting properties of new Avicel types
AU Doelker, E.; Massuelle, D.; Veuillez, F.; Humbert-Droz, P.
CS School of Pharmacy, University of Geneva, Geneva, Switz.
SO Drug Development and Industrial Pharmacy (1995), 21(6), 643-61
CODEN: DDIPD8; ISSN: 0363-9045
PB Dekker
DT Journal
LA English
AB The six Avicel products designed for compression, the classical grades PH-105, PH-103, PH-101 and PH-102, and the new Avicels PH-112 and PH-200, have been submitted to a comparative investigation for both their basic and tableting properties. According to the manufacturer all these products differ by their nominal particle size and moisture content. Basic properties of the powders were first detd., namely moisture content (loss on drying and Karl Fischer titrn.), particle size and shape (sieving and image anal.), densities (true bulk and tap densities, Hausner ratio) and flow properties (vibratory hopper technique). As tableting properties, the compactability of the powders and the effect of adding a hydrophobic lubricant (0.5% magnesium stearate) on the compact strength were evaluated by prepg. compacts at a given applied pressure using a hydraulic press. Wt. and dimensional variations were assessed by prepg. tablets at a target crushing strength of 70 Newtons on a high speed machine. The comparison of the conventional Avicel PH grades showed that Avicel PH-105 differed markedly in its properties (high compressibility on tapping, high compactability, in acceptable tablet wt. variability and very poor disintegrating properties) from the other grades. As to the two new Avicel PH grades, conflicting results with the literature were obtained with the low- moisture product Avicel PH-112. The authors obsd., like other authors but in contrast to manufacturer's data, values of compatibility and strength redn. ratio upon lubrication as well as of the coeff. of tablet wt. variation similar to those of the std. Avicel PH-102, of comparable particle size. This can be certainly explained by an uptake of moisture of the Avicel PH-112 powder as proved exptl. This would limit the use of this material to an air-conditioned room. The large particle size product Avicel PH-200 displayed a compactability close to that of all the other Avicel PH grades (except PH-105), but the highest susceptibility to magnesium stearate. As expected, because it is free-flowing, Avicel PH-200 gave the lowest tablet wt. variability. Addnl., the two new grades showed disintegrating

properties similar to those of Avicel PH-103, PH-102 and PH-101. Finally, one should bear in mind that the small differences reported here may not be significant because of substantial interbatch variability.
CC 63-5 (Pharmaceuticals)
IT Humidity
Particle size
(physicochem. and tableting properties of Avicel products)
IT Pharmaceutical dosage forms
(tablets, physicochem. and tableting properties of Avicel products)

L175 ANSWER 10 OF 19 HCA COPYRIGHT 2008 ACS on STN
AN 120:86395 HCA Full-text
OREF 120:15293a,15296a
TI Air conditioning of a hard gelatin capsule plant
AU Sule, S.M.
CS Ahmedabad, India
SO Actes Congr. Int. Froid, 18th (1991), Volume 3, 1440-1446
Publisher: 18th Int. Congr. Refrig., Saint-Hyacinthe, Que.
CODEN: 59HQA7
DT Conference
LA English
AB The effect of variation in the dry-bulb temp. and relative humidity on the properties of capsules while molding was detd. and the air quantity and conditions of air that need to be regulated to control drying were defined.
CC 63-8 (Pharmaceuticals)
ST air conditioning hard gelatin capsule plant
IT Capsules
(hard gelatin, properties of, air conditioning parameters effect on)
IT Air conditioning
(properties of hard gelatin capsules in relation to parameters of)
IT Pharmaceutical dosage forms
(capsules, hard gelatin, properties of, air conditioning parameters effect on)

L175 ANSWER 11 OF 19 HCA COPYRIGHT 2008 ACS on STN
AN 119:80221 HCA Full-text
OREF 119:14243a,14246a
TI Method of manufacture of tablets for the preparation of parenteral solutions
IN Baluch, Jozef; Zatloukalova, Viera; Chalabala, Milan; Martinovic, Karol
PA Univerzita Komenskeho, Czech.

SO Czech., 4 pp.
CODEN: CZXXA9
DT Patent
LA Slovak
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CS 275206	B2	19920219	CS 1989-4073	19890703 <--

PRAI CS 1989-4073 19890703 <--

AB The procedure is suitable for agents with properties not conducive to good tablet formation. A soln. of dextran 40 or dextran 70 is sprayed on the powd. agents and dried by bacteriol. filtered air at 30-110°. The amt. of dextran used varies 0.2-10% of the mass of drugs. The resulting dry granulate can be used for tablet pressing. Examples for the prepn. of tablets of NaCl, glucose, dextran-70, mannitol, and procaine chloride are given. The tablets can be surface-coated with macrogol.

IC ICM A61K009-20
CC 63-6 (Pharmaceuticals)
ST tablet infusion soln drug formulation
IT Pharmaceutical dosage forms
(infusions, tablets for prepn. of)
IT Pharmaceutical dosage forms
(tablets, coated, for prepn. of infusion soln.)
IT 9004-54-0, Dextran, biological studies
(tablets manufd. with, for infusion soln. prepn.)

L175 ANSWER 12 OF 19 HCA COPYRIGHT 2008 ACS on STN
AN 114:129130 HCA Full-text
OREF 114:21843a,21846a
TI Processes for the preparation of pharmaceutical compositions containing bromocriptine having high stability and related products
IN Moro, Luigi; Fiori, Achille; Natali, Alberto
PA Poli Industria Chimica S.p.A., Italy
SO Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	EP 391374	A2	19901010	EP 1990-106403	199004 04 <--
	EP 391374	A3	19920701		
	EP 391374	B1	19941207		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	US 5066495	A	19911119	US 1990-502520	199003 30 <--
	ES 2029776	T3	19950201	ES 1990-106403	199004 04 <--
	DD 293961	A5	19910919	DD 1990-339473	199004 05 <--
	DD 293961	B5	19941110		
PRAI	IT 1989-20063	A	19890407 <--		

AB Bromocriptine tablets or capsules are prepd. wherein the active ingredient is protected by inclusion in an excipient or by sepd. granulation of the excipients and mixing granulate with a mixt. of the active ingredient and an excipient having low moisture content. Bromocriptine mesylate 28.7 g was dissolved in 80% EtOH, crosslinked polyvinylpyrrolidone 42 g was wet with the soln., and the mixt. was dried under forced circulation of air at 60°. The powder was passed through a sizing net and admixed with lactose 1, 158.2, starch 140, maleic acid 20, colloidal silicic acid 3.5, and Mg stearate 7 g. The mixt. was pressed into tablets. The blistered tablets showed no signs of coloration after 6 mo storage at room temp.; unblistered tablets kept in a glass container for 45 days at 60° showed a very light darkening.

IC ICM A61K009-20
ICS A61K009-48; A61K047-30; A61K031-48

CC 63-6 (Pharmaceuticals)

IT Pharmaceutical dosage forms
(capsules, of bromocriptine, stability of)

IT Pharmaceutical dosage forms
(tablets, of bromocriptine, stability of)

L175 ANSWER 13 OF 19 HCA COPYRIGHT 2008 ACS on STN
AN 101:71384 HCA Full-text
OREF 101:11007a,11010a

TI Effervescent granulates processed into effervescent tablets
IN Gergely, Gerhard; Gergely, Thomas; Klinger, Irmgard
PA Austria
SO Austrian, 7 pp.
CODEN: AUXXAK
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI AT 374348	B	19840410	AT 1980-3429	19800701 <--
AT 8003429	A	19830915		

PRAI AT 1980-3429 19800701 <--

AB An effervescent powder, which can be pressed into tablets, is manuf. by mixing a cryst. carboxylic acid and CO32- or HCO3-, and then adding water to cause a partial reaction between the 2 compds. This covers the carboxylic acid crystals with the resp. salt and reduces the possibility of spontaneous reaction between the acid and NaHCO3 during storage of the mixt. The reaction was controlled by carrying it out in an evacuated vessel, and estg. the amt. of water needed by the amt. of CO2 evolved. Thus, 30 kg citric acid [77-92-9] was heated at 60° in a 100 L vacuum container for 5 min and then held briefly under vacuum to remove residual moisture. Then 10 kg NaHCO3 was added and the mixt. heated at 60°. A headspace of 50 L remained in the vessel. The vessel was evacuated and 210 mL water was added. The evolved CO2, measured by change of pressure in the vessel, reached 81 g and indicated that 38.5 g mono-Na citrate had formed on the citric acid crystals. This procedure was repeated twice, with relatively little CO2 evolution during the final procedure. The stabilized mixt. was then ground, treated with vitamins and flavorings, and pressed into tablets.

IC A23L002-40
CC 17-6 (Food and Feed Chemistry)
Section cross-reference(s): 63
IT Beverages
Pharmaceuticals
(effervescent granules for prepn. of)

L175 ANSWER 14 OF 19 HCA COPYRIGHT 2008 ACS on STN
AN 70:109142 HCA Full-text
OREF 70:20419a,20422a
TI Protopectin-cellulose mixtures of plant origin as aids in direct tableting. I. Production and dispersant

properties of the preparation from sugar beet and fodder beet roots
AU Sykulska, Zofia
CS Akad. Med., Lodz, Pol.
SO Herba Polonica (1968), 14(3), 155-62
CODEN: HPBIA9; ISSN: 0018-0599
DT Journal
LA Polish
AB Peeled beet roots were crushed, placed in a 0.1% Na2S2O4 soln. to inactivate tyrosinase, squeezed out, and washed to neg. reaction for sucrose. After each washing the pulp was suspended in excess water, agitated 5 min., and squeezed out. The first 2 washings were made with 0.1% Na2S2O4 soln. After the last washing the product was pressed out and extd. twice during 30 min. with a 4-fold amt. of MeOH under reflux. The mass was then squeezed out, crushed, and dried at room temp. The raw product was milled and sifted through a sieve of mesh diam. 0.1 mm. To purify and bleach the product, it was suspended in a 20-fold amt. of water, the suspension was deaerated 10 min. in vacuo, and 0.2% Na2S2O4 (based on H2O wt.) was added. After 5 min. the product was squeezed out and washed 5 times. The residue was mixed twice for 5 min. with a 4-fold amt. of MeOH, filtered off, washed 3 times with MeOH, and left to dry on a filter paper at a relative humidity of 55-65%. The dried product was again milled and sifted to give .apprx.5(sugar beets) or .apprx.3% (fodder beets) of a white, odorless, tasteless, and easily flowing powder. The addn. of the powder to 10 drugs gave tablets with excellent mech. properties and short disintegration time, without the necessity of preliminary granulation. For tableting ascorbic acid, only powder of low sol. pectin content was suitable. The powder proved unsuitable for tableting highly alk. drugs such as Na phenobarbital, and was very useful for aerophilic powders (phenacetin), and quinine sulfate. Moreover, properties of the tablets underwent little changes on storage up to 10 months. Detn. of the liberation rate of aminophenazone and ascorbic acid from the tablets showed that the complete dissoln. of both drugs occurred after 4 and 3 min., resp. The rates decreased only slightly after a 3-month storage.
CC 63 (Pharmaceuticals)
IT Beets
Sugar beets
(in tablet manuf.)

L175 ANSWER 15 OF 19 HCA COPYRIGHT 2008 ACS on STN
AN 69:30122 HCA Full-text
OREF 69:5643a,5646a
TI Directly compressed low-density crystalline sorbitol pharmaceutical tablets
IN Palermo, Blaze T.
PA Miles Laboratories, Inc.

SO U.S., 7 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3384546	A	19680521	US 1965-459896	19650528 <--
BR 6679980	D0	19731023	BR 1966-179980	19660527 <--

PRAI US 1965-459896 A 19650528 <--

AB Tablets are compressed from a mixt. in which 25-100% of the excipient is low density, cryst. sorbitol. Thus, dry ingredients are added (in increasing order of their free moisture content) and blended to give a mixt. contg. citric acid 17.5, Na ascorbate 64.7, mannitol 118, thiamine mononitrate (33.3%) 6.6, riboflavine (25%) 10.5, niacinamide (33.3%) 60, pyridoxine-HCl 1.05, Na cyclamate 7.5, sorbitol (cryst. granules, bulk density 0.53-0.545 g./cc., 16-40 mesh) 144, Mg stearate 6, vitamins A and D 9.25, vitamin A 2.25, vitamin B12 0.115, rice starch 25, Na saccharin 0.75, and color and flavoring 6.25 mg./tablet. This blend is directly compressed on a conventional rotary press to give non-gritty chewable multiple vitamin tablets (sorbitol comprising 55% of the excipient) which compare favorably with control tablets (contg. all-mannitol excipient) in mouthfeel, consistency, low rate of moisture pickup, and chem. stability against deterioration under normal temp. and humadity conditions encountered in shipping and storage. Similar results are obtained with excipients composed of 100% sorbitol or blends of 25-55% sorbitol and mannitol, dextrose, or lactose. The compn. is used to prep. chewable vitamins, antacids, and analgesics.

INCL 167082000
CC 63 (Pharmaceuticals)
ST sorbitol tablet; vitamin tablet sorbitol; tablet sorbitol
IT Tablets
(manuf. of directly compressed)
IT Vitamins, biological studies
(tablets (directly compressed) contg.)
IT 50-70-4
(tablets (directly compressed) contg.)

L175 ANSWER 16 OF 19 HCA COPYRIGHT 2008 ACS on STN
AN 68:62653 HCA Full-text
OREF 68:12134h,12135a
TI Stability of acetylsalicyclic acid tablets under various conditions of air humidity
AU Wisniewski, Wladyslaw; Piasecka, Hanna
CS Akad. Med., Warsaw, Pol.
SO Acta Poloniae Pharmaceutica (1967), 24(3), 291-6
CODEN: APPHAX; ISSN: 0001-6837
DT Journal
LA Polish
AB Decompn. of acetylsalicylic acid (I) mixed with various filling substances and pressed into tablets with the same fillers was surveyed under different air humidity conditions by detg. colorimetrically salicylic acid in the reaction with NH4Fe(SO4)2. The decompn. increased with humidity and was as high as 100% in mixts. contg. I 0.5, talc 0.075, and MgO 0.075 parts after 15 months at relative air humidity of 93%. Pure I and mixts. and tablets prepd. according to Polish Pharmacopeia III (I 0.5, starch 0.1, and talc 0.05 parts) showed, under similar storage conditions, only 0.15% decompn. Intermediate % decompn. values were reported for mixts. and tablets prepd. with CaCO3, MgCO3, and Mg stearate.
CC 63 (Pharmaceuticals)
ST DRUG STABILITY; ACETYLSALICYLIC ACID STABILITY
IT 50-78-2, properties
(stability of, humidity effect on)

L175 ANSWER 17 OF 19 HCA COPYRIGHT 2008 ACS on STN
AN 47:57039 HCA Full-text
OREF 47:9654d-g
TI Gelatin
PA Council of Scientific and Industrial Research
DT Patent
LA Unavailable
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 45583		19530528	IN	

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AB Hide trimmings (20 parts by wt.) are thoroughly washed in a drum washer and limed with 113 parts by wt. of 3° B.acte.e. lime slurry for 6 weeks. The limed hide is delimed in a specially designed paddle washer with H2O. It is then washed with HCl, and finally the excess acid is washed away with H2O. The stock is extd. with H2O in an Al or stainless steel extractor. Three exts. are taken at 55°, 65°, and 85°, resp., at a duration of 4 hrs. each. The pH during

extn. is maintained at 6.0. The exts. are filtered in a wooden filter press, concd. to 15% gelatin soln. in a long-tube vacuum evaporator. The concentrate is decolorized with active C and filtered in a wooden filter press. It is then set to a jelly in a cold room maintained at about 50°, cut into suitable sizes, and dried in a countercurrent air drier: the inlet temp. of air is maintained at 45°. The humidity of the incoming air is controlled. Gelatin may also be obtained by the above process from treated hides, skins, or skin cutting. Gelatin obtained by the above process has extensive applications in industry, such as the photographic film industry, the pharmaceutical industry, and the food industry. It may be used in the manuf. of capsules, pastilles, suppositories, candy, jelly, or ice cream.

CC 29 (Leather and Glue)

IT Food
Pharmaceuticals
(gelatin for)

L175 ANSWER 18 OF 19 HCA COPYRIGHT 2008 ACS on STN

AN 0:206895 HCA Full-text

TI The preparation of the Betulins by sublimation. [machine translation]

AU Wheeler, J.

SO The pharm. Journ. (1899), 32, 738-39
From: Chem. Zentr., 1900, I, 353-354

DT Journal

LA Unavailable

AB [Machine Translation of Descriptors]. Betulin has the formula C36H6008, gives and heated up at 130° C. an anhydride, it is tasteless and odorless, melts slowly at 257.8° and sublimates easily in an air flow. It is neither with acid, nor alkalis, it is insoluble at compounds in water, little soluble in alcohol, easily soluble in ether, turpentine oils and almond oil. It separates fast and calmly in oil of vitriol, which hardens and tartaric acid solution on water additive. Author represents the Betulin, by mixing, in tablet or Block-form pressing the tough epidermis with 1 to 8% potassium nitrate powdered by Betula alba and burning in closed chambers under appropriate control of the air access without flame. The observed Betulin vapor serves for preparation of thin film on different materials, as Baud things, plasters, etc., it affects those things as antiseptic.

CC 17 (Pharmaceutical Chemistry)

L175 ANSWER 19 OF 19 HCA COPYRIGHT 2008 ACS on STN

AN 0:206894 HCA Full-text

TI The preparation of the Betulins by sublimation. [machine translation]

AU Wheeler, J.

SO The pharm. Journ. (1899), 32, 494
From: Chem. Zentr., 1900, I, 353-354
DT Journal
LA Unavailable
AB [Machine Translation of Descriptors]. Betulin has the formula C36H6008, gives and heated up at 130° C. an anhydride, it is tasteless and odorless, melts slowly at 257.8° and sublimates easily in an air flow. It is neither with acid, nor alkalis, it is insoluble at compounds in water, little soluble in alcohol, easily soluble in ether, turpentine oils and almond oil. It separates fast and calmly in oil of vitriol, which hardens and tartaric acid solution on water additive. Author represents the Betulin, by mixing, in tablet or Block-form pressing the tough epidermis with 1 to 8% potassium nitrate powdered by Betula alba and burning in closed chambers under appropriate control of the air access without flame. The observed Betulin vapor serves for preparation of thin film on different materials, as Baud things, plasters, etc., it affects those things as antiseptic.
CC 17 (Pharmaceutical Chemistry)

=> D L176 1-12 BIB ABS HITIND

L176 ANSWER 1 OF 12 HCA COPYRIGHT 2008 ACS on STN
AN 138:326594 HCA Full-text
TI Highly compressible ethyl cellulose for tableting
IN Durig, Thomas; Hall, Ronald Haywood; Salzstein, Richard A.
PA Hercules Incorporated, USA
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003032955	A1	20030424	WO 2002-US32049	20021008

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 20030077327 A1 20030424 US 2001-977785
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US 6592901 B2 20030715

CA 2463583 A1 20030424 CA 2002-2463583
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AU 2002342012 A1 20030428 AU 2002-342012
200210
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EP 1435918 A1 20040714 EP 2002-776176
200210
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

BR 2002013288 A 20041123 BR 2002-13288
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CN 1571662 A 20050126 CN 2002-820405
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JP 2005509620 T 20050414 JP 2003-535759
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MX 2004PA03378 A 20040618 MX 2004-PA3378
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IN 2004DN00942 A 20050401 IN 2004-DN942
200404
12
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IN 2004DN03708 A 20050401 IN 2004-DN3708
200411
24
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PRAI US 2001-977785 A 20011015 <--
WO 2002-US32049 W 20021008 <--

AB A pharmaceutical dosage form compn. is composed of an Et cellulose (EC) that has an ethoxyl range lower limit of 49.6%, an a viscosity of <53 cPs and at least 1 active pharmaceutical ingredient. This dosage form is highly compressible and compactible forming harder tablets or pellets with better release retardation than comparable prior art tablets. EC materials with varying viscosities and ethoxyl percentages were blended with 1% stearic acid as a lubricant and compressed on a rotary tablet press. The 3 EC samples with an ethoxyl content with a lower limit of 25 49.65% and a viscosity <50 cPs gave tablets with clearly superior crushing strength.

IC ICM A61K009-20

CC 63-6 (Pharmaceuticals)

IT Anabolic agents
Analgesics
Antacids
Anti-AIDS agents
Anti-inflammatory agents
Antianginal agents
Antiarrhythmics
Antiasthmatics
Anticoagulants
Anticonvulsants
Antidiabetic agents
Antidiarrheals
Antiemetics
Antihistamines
Antihypertensives
Antimigraine agents
Antiobesity agents
Antipyretics
Antitumor agents
Antitussives
Coating materials
Compaction
Compressibility
Compression
Crushing strength
Decongestants
Dietary supplements
Digestive tract
Diuretics
Erythropoiesis
Expectorants
Friction
Glass transition temperature

Hyperglycemia
Hypnotics and Sedatives
Laxatives
Nausea
Particle size distribution
Psychotropics
Tocolytic agents
Vasoconstrictors
Viscosity
(highly compressible Et cellulose for tableting)
IT Anesthetics
(local; highly compressible Et cellulose for tableting)
IT Drug delivery systems
(pellets; highly compressible Et cellulose for tableting)
IT Drug delivery systems
(tablets; highly compressible Et cellulose for tableting)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L176 ANSWER 2 OF 12 HCA COPYRIGHT 2008 ACS on STN
AN 134:344498 HCA Full-text
TI The spray drying of acetazolamide as method to modify crystal properties and to improve compression behavior
AU Di Martino, P.; Scoppa, M.; Joiris, E.; Palmieri, G. F.; Andres, C.; Pourcelot, Y.; Martelli, S.
CS Department of Chemical Sciences, University of Camerino, Camerino, 62032, Italy
SO International Journal of Pharmaceutics (2001), 213(1-2), 209-221
CODEN: IJPHDE; ISSN: 0378-5173
PB Elsevier Science B.V.
DT Journal
LA English
AB Acetazolamide shows a very poor must usually be produced through a wet granulation process. However, the possibility to obtain pure acetazolamide for direct compression could be interesting for industrial application. With the scope to obtain a material for direct compression, three different crystn. methods were chosen, with respect to acetazolamide solvent soly. (a) Acetazolamide was dissolved in an ammonia soln. and then spray dried. It was possible to characterize the spherical particles as a mixt. of 2 polymorphic forms, I and II by powder x-ray diffraction study. (b) pure form I was obtained by slowly cooling to room temp. a boiling water soln. (c) pure form II, the marketed form, was obtained by neutralization of an ammonia soln. Their compression behavior was investigated firstly by a rotary press. While pure polymorphic forms I and II could not be compressed, the spray dried particles showed very good

compression properties. In fact, tablets were obtained only by spray dried particles, which show very good properties under compression and the absence of capping tendency. On the other hand, it was impossible to obtain tablets from polymorphic forms I and II, whatever compression pressures were used. In order to explain their densification mechanism, a single-punch tablet machine, equipped for the measurement of the upper punch displacement in the die, was used. From calcd. Heckel's parameters, it was demonstrated that the spray dried material shows a greater particle rearrangement in the initial stage of compression due to its spherical habit and minor wrinkledness of particle surface. The cryst. structure due to the presence of polymorphic forms I and II concur to lowering the intrinsic elasticity of the material. This fact avoids the risk of the rupturing the interparticulate bonds, which are formed during the compression, concurring to the consolidation of the tablet.

CC 63-6 (Pharmaceuticals)

IT Drug delivery systems
(tablets; spray drying of acetazolamide for modifying crystal properties and to improve compression)

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L176 ANSWER 3 OF 12 HCA COPYRIGHT 2008 ACS on STN

AN 125:67669 HCA Full-text

OREF 125:12775a,12778a

TI Force-time curves of a rotary tablet press. Interpretation of the compressibility of a modified starch containing various amounts of moisture

AU Leitritz, M.; Krumme, M.; Schmidt, P. C.

CS Dep. Pharmaceutical Technology, Eberhard-Karls Univ., Tuebingen, D-72076, Germany

SO Journal of Pharmacy and Pharmacology (1996), 48(5), 456-462
CODEN: JPPMAB; ISSN: 0022-3573

PB Royal Pharmaceutical Society of Great Britain

DT Journal

LA English

AB On a rotary tablet press, the force-time curves are segmented into three phases: the compression phase, the dwell phase during which both stress and strain are variable for plastically deforming materials and the decompression phase. The following 7 parameters were investigated: the compression area and the compression slope describing the initial phase, the area ratio and the peak offset time characterizing the dwell time, the decompression area (A4) and the decompression slope (Sld) describing the terminal phase and the total area under the force-time curve. Tablet strength, tablet porosity and in-die bulk porosity provide addnl. information for comprehensive

interpretation. The values of A4 for the 4 starch batches are not significantly different. Sld provides somewhat better information about the elastic compact recovery. In general, however, the short decompression phase seems to be inappropriate for characterization by force-time curve parameters, because it is difficult to sep. machine recovery from that of the tablet. Porosity above the porosity limit of the material was a prerequisite for plastic flow within the compact. When the porosity limit is reached, further densification remains elastic and leads to a reduced compact strength during expansion. The area ratio, as a robust in-process control parameter for plastically flowing formulations, is suggested as a means of preventing this effect.

CC 63-8 (Pharmaceuticals)

ST moisture tablet compressibility; starch moisture tablet compressibility

IT Compression and Compressibility
Porosity
(compressibility of tablets contg. various amts. of moisture)

IT Pharmaceutical dosage forms
(tablets, compressibility of tablets contg. various amts. of moisture)

IT 9005-25-8, Starch, biological studies
(compressibility of tablets contg. various amts. of moisture)

L176 ANSWER 4 OF 12 HCA COPYRIGHT 2008 ACS on STN

AN 124:185396 HCA Full-text

OREF 124:34135a,34138a

TI Studies on direct compression of dry extract formulations by means of an internal and external lubrication system

AU Laich, T.; Reher, M.; Kissel, T.; Voss, G. M.

CS Inst. Pharm. Technol. Biopharm., Phillips-Univ., Marburg, D-35032, Germany

SO Pharmazeutische Industrie (1995), 57(11), 950-8
CODEN: PHINAN; ISSN: 0031-711X

PB Cantor

DT Journal

LA German

AB The internal phase lubrication and a new system of spray-coating of all friction-loaded tooling surface with a lubricant suspension were compared by direct compression of dry exts. of Passiflora incarnata, Humulus lupulus, thymus vulgaris, or lactose as placebo mixt. on an instrumented rotary press. The pressure-hardness-relation of tableting masses, the tendency to cap or laminate, and the coating qualities of the tablets were investigated. The spray-coating system increased the max. loading capacity of the direct compression

formula, reduced the capping tendencies and the dry binder amt. by 17%. A faster disintegration of the tablets was not obsd. The phys. properties of the exts. had an extreme influence on the compression characteristics of the mixts. during the tableting. The flow properties of the tableting masses during tableting correlated with the initial moisture uptake of the exts.

CC 63-6 (Pharmaceuticals)

IT Pharmaceutical dosage forms
(tablets, direct compression of dry ext. formulations by means of internal and external lubrication system)

IT Pharmaceutical dosage forms
(tablets, compressed, direct compression of dry ext. formulations by means of internal and external lubrication system)

L176 ANSWER 5 OF 12 HCA COPYRIGHT 2008 ACS on STN

AN 121:238289 HCA Full-text

OREF 121:43305a,43308a

TI Comparison of two microcrystalline cellulose brands for the direct compression of hydrochlorothiazide tablets

AU Wambolt, E.; McKnight, C.; Turkoglu, M.; Sakr, A.

CS Coll. Pharm., Univ. Cincinnati, Cincinnati, OH, 45267, USA

SO Pharmazeutische Industrie (1993), 55(11), 1046-51
CODEN: PHINAN; ISSN: 0031-711X

DT Journal

LA English

AB The effect of storage on tablets formulated with 2 different brands of coarse microcryst. cellulose (MCC), MCC-1 and MCC-2, was studied. To compare the 2, 25 mg hydrochlorothiazide tablets were prepd. by direct compression, using a 50:50 blend of MCC and anhyd. lactose, incorporating crosslinked PVP, croscarmellose, or sodium starch glycolate and magnesium stearate. Tablets (150 mg) were compressed on a rotary tablet press and were evaluated for wt., thickness, hardness, friability, disintegration time, and dissoln. (U.S.P.) initially, and after 9 mo storage at room temp. It was found that, in a majority of the batches, tablets made with MCC-2 were significantly harder than those made with MCC-1. This disparity in hardness appears to be reflected in differences in disintegration time and drug dissoln. rate from comparable tablet batches. MCC-2 tablets formulated without disintegrant exhibited a disintegration time significantly longer (at least 50% longer) than those contg. MCC-1. The trend across all of the tablet batches, regardless of disintegrant used, was that MCC-2 tablets exhibited a slower dissoln. rate than their MCC-1 counterparts. Upon storage, statistically significant changes in hardness were seen in some MCC-2 batches, but none of the MCC-1 batches. The results indicate that MCC-1 and MCC-2 may not perform identically.

CC 63-6 (Pharmaceuticals)
IT Pharmaceutical dosage forms
(tablets, microcryst. cellulose brands comparison for direct compression of hydrochlorothiazide tablets)

L176 ANSWER 6 OF 12 HCA COPYRIGHT 2008 ACS on STN
AN 121:91635 HCA Full-text
OREF 121:16315a,16318a
TI Moisture-activated dry granulation in a high shear mixer
AU Christensen, L. H.; Johansen, H. E.; Schaefer, T.
CS Dep. Pharm. Development, Nycomed Dak A/S, Copenhagen, DK-2300, Den.
SO Drug Development and Industrial Pharmacy (1994), 20(14), 2195-213
CODEN: DDIPD8; ISSN: 0363-9045
DT Journal
LA English
AB The applicability of a 25-L high shear mixer for moisture -activated dry granulation was examd. Microcryst. cellulose, potato starch or a mixt. of 50% m/m of each was used as moisture absorbing material. The effects of water content, wet massing time, moisture absorbing material and dry mixing time on the size distribution, and the compressibility of the granulations were investigated. Tablets were compressed on a single punch press from all the granulations and on a rotary press from a few of the granulations.
CC 63-6 (Pharmaceuticals)
ST moisture activation dry granulation shear mixer
IT Mixing apparatus
(high shear, moisture-activated dry granulation in, properties of tablets and granules in relation to)
IT Compression and Compressibility
(of granules, prepd. by moisture-activated dry granulation in high shear mixer)
IT Particle size
(of granules, prepd. by using moisture-activated dry granulation in high shear mixer)
IT Crushing strength
(of tablets, prepd. by using moisture -activated dry granulation in high shear mixer)
IT Granulation
(dry, of pharmaceutical powders, moisture -activated, in high shear mixer, properties of tablets and granules in relation to)
IT Pharmaceutical dosage forms
(granules, properties of, prepd. by using moisture -activated dry granulation in high shear mixer)
IT Pharmaceutical dosage forms
(tablets, properties of, prepd. by using

moisture-activated dry granulation in high shear mixer)
IT 50-06-6, Phenobarbital, miscellaneous 63-42-3, Lactose 557-04-0, Magnesium stearate 9003-39-8, Povidone 9005-25-8, Starch, miscellaneous 14807-96-6, Talc, miscellaneous
(dry granulation of formulations contg., moisture-activated, in a high shear mixer)
IT 9004-34-6, Cellulose, miscellaneous
(microcryst., dry granulation of formulations contg., moisture-activated, in a high shear mixer)

L176 ANSWER 7 OF 12 HCA COPYRIGHT 2008 ACS on STN
AN 121:17919 HCA Full-text
OREF 121:3299a,3302a
TI Characterization of Wet Granulation Process Parameters Using Response Surface Methodology. 1. Top-Spray Fluidized Bed
AU Lipps, Douglas M.; Sakr, Adel M.
CS College of Pharmacy, University of Cincinnati Medical Center, Cincinnati, OH, 45267-0004, USA
SO Journal of Pharmaceutical Sciences (1994), 83(7), 937-47
CODEN: JPMSAE; ISSN: 0022-3549
DT Journal
LA English
AB Randomized full-factorial designs (32) were used to investigate the effects of processing conditions in the top-spray fluidized bed (TSFB) on the granulation of acetaminophen powder (USP) using 5% polyvinylpyrrolidone (wt./wt.) as the binder. Measured granule properties included the following: mean size and size distribution, sp. surface area, bulk d., tapped d., flow rate through an orifice, angle of repose, residual moisture content, and percent overs (>2 mm). The granules were then compressed (500, 1000, 1500 lbs) into tablets (9-mm shallow concave) using an instrumented rotary press and analyzed for both phys. properties and drug-release characteristics. All exptl. batches were run in triplicate to reduce the possibility of erroneous results and to increase the confidence in the resulting empirical relationships derived using response-surface methodol. Measured responses were then related to process parameters using two-factor and three-factor linear interactions and quadratic regression models. These models were used to generate three-dimensional response surfaces for use in the final analyses. Coeffs. of detn. (R2) ranging from 0.08 to 0.81 were obtained, indicating that only a portion of the variation in the data could be explained by the changes in process parameter settings during granulation and tableting. The best overall model fits were obsd. for mean granule size, size distribution, bulk d., tapped d., percent drug dissoln., tablet disintegration time, and tablet friability.
CC 63-6 (Pharmaceuticals)
IT Particle size

(of drugs manufd. by wet granulation with top-spray fluidized bed)
IT Solution rate
(of drugs, from dosage forms manufd. by wet granulation in top-spray fluidized bed)
IT Pharmaceutical dosage forms
(tablets, wet granulation by top-spray fluidized bed in relation to)

L176 ANSWER 8 OF 12 HCA COPYRIGHT 2008 ACS on STN
AN 116:221485 HCA Full-text
OREF 116:37381a,37384a
TI Infrared imaging of pharmaceutical materials undergoing compaction
AU Bechard, Simon R.; Down, G. R. B.
CS Merck Frosst Cent. Ther. Res., Pointe-Claire-Dorval, QC, H9R 4P8, Can.
SO Pharmaceutical Research (1992), 9(4), 521-8
CODEN: PHREEB; ISSN: 0724-8741
DT Journal
LA English
AB The goal of this study was to use IR thermog. as a new technique to investigate the heat released during compaction and consolidation of pharmaceutical powders and granules. Real-time temp . measurements without phys. contact with tablets were provided by a highly sensitive (±0.1° at 30°) IR camera (Agema IR Systems, Model 470 with CM-SOFT software). High-resoln. images were captured at the takeoff point, i.e., less than 1 s after compaction, stored on floppy disks, and then analyzed on a regular PC equipped with a VGA color monitor. Thermal surface profiles of tablets were obtained with high geometric and temp. resoln. Reproducibility of the camera readouts was better than 3%. The model granulation used was a direct compression blend of microcryst. cellulose, spray-dried lactose, and magnesium stearate. This blend was compressed using an instrumented Korsch PH106 rotary press fitted with 1 station of 19.1 + 7.9-mm (0.750 + 0.312-in.) capsule-shaped tools. The effects of compaction force (6-20 kN), rate (130- to 360-nsec contact time), and lubricant level (0.5 and 1.0%) on postcompaction temp. rise, caused by heat released during compaction, were investigated. The presence and location of nonhomogeneous heat distribution were assessed as well. Results have shown that the heat released during compaction increases with compaction force. Tablet surface temps. of 33.8° were obsd. at 20 kN compaction force in contrast to 29.5° at 6.7 kN. The compression rate, as detd. by the upper punch contact time did not have any significant effect on the heat released during compaction at 15-kN force. However, magnesium stearate level had a significant effect on the heat released during a compaction run. Tablets lubricated with

1.0% magnesium stearate had surface temps. of 39-40° after a 20-min run time, as opposed to 50-51° for tablets lubricated with 0.5% magnesium stearate. Hot spots were seen at tablet edges where the die-wall friction occurs. Tablet cross-sectional thermal profiles revealed a 3-4° temp. gradient across the tablet. These expts. show that IR imaging is a unique tool for semiquant. evaluation of heat released during compaction because it provides direct visualization with good temp. resoln. of the heat evolved during the process.

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 69

ST compaction drug heat IR imaging; lubricant drug compaction heat

IT Compaction
(of pharmaceutical granules and powders, heat release in, IR imaging study of)

IT Heat
(release of, during compaction of pharmaceutical granules and powders, lubricant effect on, IR imaging study of)

IT Imaging
(IR, heat release during compaction of pharmaceutical granules and powders study by, lubricant effect on)

IT Pharmaceutical dosage forms
(granules, compaction of, heat release during, lubricant effect on, IR imaging study of)

IT Pharmaceutical dosage forms
(powders, compaction of, heat release during, lubricant effect on, IR imaging study of)

IT Pharmaceutical dosage forms
(tablets, compaction of granules and powders in prepn. of, heat release during, lubricant effect on, IR imaging study of)

L176 ANSWER 9 OF 12 HCA COPYRIGHT 2008 ACS on STN
AN 113:218074 HCA Full-text
OREF 113:36728h,36729a
TI Production of spray dried rice starch and its utilization in pharmaceutical industry
AU Varavinit, Saiyavit; Mitrevej, Ampol
CS Fac. Sci., Mahidol Univ., Bangkok, Thailand
SO Microbial Utilization of Renewable Resources (1989), 6, 158-62
CODEN: MURRE6
DT Journal
LA English
AB Spray dried rice starch (SDRS) was prepd. by spray drying of rice starch under suitable conditions. SEM revealed that particle of SDRS were spherical and made up entirely agglomerates of rice starch

grains. Tablet properties of SDRS were studied and compared with those of three com. available direct compression fillers. Hardness, friability, and disintegration of the tablets were evaluated. SDRS was inferior to only one of them. A blend of propranolol-HCl and SDRS was tableted on an rotary tablet press. Segregation did not occur over a two-h period. To demonstrate the uniform distribution of low-dose drug, a mixt. of SDRS and chlorpheniramine maleate were prepd. at 4% of the drug. The tablets were assayed for the content uniformity and found to be excellent. Since direct compression process avoided the use of heat and moisture which were normally employed in wet granulation process, aspirin which is a heat- and moisture -sensitive drug was formulated with the use of SDRS. The tablets obtained were satisfactory. Thus, SDRS can be used successfully as a filler in direct compression tableting.

CC 63-6 (Pharmaceuticals)

ST spray drying starch pharmaceutical; rice starch pharmaceutical; tablet rice starch

IT Solution rate
(of drugs, from tablets contg. spray-dried rice starch)

IT Pharmaceutical dosage forms
(tablets, fillers for direct compression of, spray-dried rice starch as)

IT 9005-25-8P, Starch, uses and miscellaneous
(spray-dried, prepn. of, for drug compression tablets)

L176 ANSWER 10 OF 12 HCA COPYRIGHT 2008 ACS on STN

AN 107:242396 HCA Full-text

OREF 107:38875a,38878a

TI Densification of N-halohydantoin compositions and additives into water treatment tablets

IN Puzig, Edward H.

PA Great Lakes Chemical Corp., USA

SO U.S., 8 pp.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 4677130	A	19870630	US 1985-785210	19851007 <--

PRAI US 1985-785210 19851007 <--

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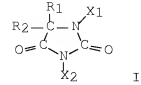

I

AB Water treatment tablets contg. N-halohydantoin compds. (I; where R, R2 = H or lower alkyl groups and X1, X2 = Br, Cl, and H where at least one is a halogen) are manufd. without oven drying by blending dry particulate I with dry particulate alkali metal or alk. earth metal salt additives 0.5-3 wt.%, tableting the mixt. contg. <5% water in a Stokes rotary press, and aging the tablets at room temp., giving tablets which can withstand automated packaging and handling. Examples showed optimum green (unaged) crush strengths for 1-bromo-3-chloro-5,5-dimethylhydantoin (BCDMH) tablets contg. particle size -10 to +20 sieve classification, water content .apprx.1.5%, and additive (Na2CO3) concn. .apprx.3 wt.%, where the additive did not affect the tablet dissoln. rate. Aging at room temp. for ≥24 h hardened the tablets, as shown by tablets contg. dried BCDMH and Na metasilicate nonhydrate 3 wt.% which had green crush strength 51 and aged (24-h) crush strength 100 psi.

IC C07D403-30; A61K033-22; A61K031-41; A01N059-14

INCL 514389000

CC 61-5 (Water)
Section cross-reference(s): 5

ST tablet manuf water disinfection; halohydantoin tablet water disinfection

IT Bactericides, Disinfectants, and Antiseptics
(N-halohydantoin tablets as, manuf. of, for water disinfection)

IT Borates
Carbonates, uses and miscellaneous
Phosphates, uses and miscellaneous
Silicates, uses and miscellaneous
(N-halohydantoin tablets contg., manuf. of, for water disinfection)

IT Water purification
(disinfection, N-halohydantoin tablets for, manuf. of)

IT Carbonates, uses and miscellaneous
(hydrogen, N-halohydantoin tablets contg., manuf. of, for water disinfection)

IT 497-19-8, Carbonic acid disodium salt, uses and miscellaneous
1333-73-9 1344-09-8 3313-92-6 5968-11-6 6132-02-1
6834-92-0 7439-93-2D, Lithium, salts 7439-95-4D, Magnesium, salts 7440-09-7D, Potassium, salts 7440-23-5D, Sodium, salts 7440-66-6D, Zinc, salts 7440-70-2D, Calcium, salts 10213-79-3 11130-11-3
(N-halohydantoin tablets contg., manuf. of, for water disinfection)

L176 ANSWER 11 OF 12 HCA COPYRIGHT 2008 ACS on STN
AN 106:38460 HCA Full-text
OREF 106:6345a,6348a
TI A method for evaluating the corrosion potential of a tablet press turret by drug substances, granulations or powder blends
AU Chrzanowski, F. A.; Kolod, I. M.; Ahlswede, B. A.; Fegely, B. J.
CS Chem. Pharm. Dev., McNeil Pharm., Spring House, PA, 19477-0776, USA
SO Drug Development and Industrial Pharmacy (1986), 12(14), 2381-5
CODEN: DDIPD8; ISSN: 0363-9045
DT Journal
LA English
AB A preformulation test was developed in which the corrosion potential of drug substances, granulations or powder blends could be evaluated. Abrasion by the powder on a metal plate simulating the abrasion occurring during the rotation of a rotary tablet press turret was crit. The method demonstrated the effect of high and moderate relative humidities upon a particular granulation which was known to corrode a turret during tablet manuf.
CC 63-8 (Pharmaceuticals)
ST corrosion tablet press turret drug
IT Humidity
(corrosion of tablet press turret by drug substances and granules and powder blends in relation to)
IT Corrosion
(of tablet press turret, drug substances and granulation and powder blends effect on)
IT Presses
(turret, tablet, corrosion of, drug substances and granulation and powder blends effect on)
IT Pharmaceutical dosage forms
(granules, corrosion of tablet press turret by)
IT Pharmaceutical dosage forms
(powders, corrosion of tablet press turret by)
IT Pharmaceutical dosage forms
(tablets, presses for, corrosion of turrets of, drugs and granules and powders effect on)

L176 ANSWER 12 OF 12 HCA COPYRIGHT 2008 ACS on STN
AN 94:197492 HCA Full-text
OREF 94:32247a,32250a
TI Manufacturing of suppositories by compression
AU De Buman, A.; Riva, A.; Surer, H. R.; Steiger, M.; Sucker, H.
CS Pharm. Forsch.- und Entwickl., Sandoz-Wander A.-G., Basel, Switz.
SO Pharmazeutische Industrie (1981), 43(3), 276-8
CODEN: PHINAN; ISSN: 0031-711X
DT Journal
LA German
AB The compression of suppositories on rotary presses is possible under industrial conditions if the compression temp. can be lowered to 0-10° by cooling the punches and the dies, as well as air in the mantle of the machine. A simple sinter or melting granulation of the active principle with the suppository base without binding agent is possible if the appropriate quality of hard fat is used. The yield of the machine can reach up to 100,000 suppositories/h if the flowing quality of the granulate is sufficient. The phys. and biopharmaceutic characteristics of the suppositories manufd. in this way are at least equal to those manufd. by the pour molding procedure. Among the various hard fats, those with a low content of short-chain (<C10) fatty acids and a high content of hydroxy fatty acids seem to be more propitious; the latter, however, are not required. The advantages of this procedure are: use of the normal equipment for tablet manuf., higher productivity, no thermal stress, no demixing, fewer phys. incompatibilities than with the melting procedure; the disadvantage is individual packaging of each drug dosage form.
CC 63-5 (Pharmaceuticals)

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=> D L172 1-22 MAX

L172 ANSWER 1 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 2008-G32344 [40] WPIX Full-text
ED 20080624
CR 1998-271724; 2005-121245
DNC C2008-201391 [40]
TI Treating secretory diarrhea, involves orally administering pharmaceutical composition containing aqueous soluble proanthocyanidin polymer composition isolated from Croton species or Calophyllum species, to animals, including humans
DC A96; B04
IN BALWANI G P; CHAN J W; KHANDWALA A S; ROZHON E J; SABOUNI A; SESIN D F
PA (NAPO-N) NAPO PHARM INC
CYC 1
PI US 7341744 B1 20080311 (200840)* EN 31[9]
ADT US 7341744 B1 CIP of US 1996-730772 19961016; US 7341744 B1 Cont of US 1998-66989 19980423; US 7341744 B1 US 2000-712033 20001114
PRAI US 2000-712033 20001114
US 1996-730772 19961016
US 1998-66989 19980423
IPCI A01N0065-00 [I,A]; A01N0065-00 [I,C]
IPCR A61K0031-352 [I,C]; A61K0031-353 [I,A]; A61K0031-74 [I,C]; A61K0031-765 [I,A]; A61K0009-28 [I,A]; A61K0009-28 [I,C]; A61K0009-50 [I,A]; A61K0009-50 [I,C]
AB US 7341744 B1 UPAB: 20080624

NOVELTY - Treating secretory diarrhea in animals, including humans, involves orally administering 0.1-100 mg/kg/day of a pharmaceutical composition to a non-human animal chosen from bovine, ovine, swine, poultry, equine, canine and feline animals or human suffering from secretory diarrhea. The pharmaceutical composition contains an aqueous soluble proanthocyanidin polymer composition isolated from a Croton sp. or Calophyllum sp..

DETAILED DESCRIPTION - Treating secretory diarrhea in animals, including humans, involves orally administering 0.1-100 mg/kg/day of a pharmaceutical composition to a non-human animal chosen from bovine, ovine, swine, poultry, equine, canine and feline animals or human suffering from secretory diarrhea. The pharmaceutical composition contains an aqueous soluble proanthocyanidin polymer composition isolated from a Croton sp. or Calophyllum sp.. The aqueous soluble proanthocyanidin polymer composition treats secretory diarrhea and formulated to protect the aqueous soluble proanthocyanidin polymer composition from the stomach environment in a controlled release preparation, and carrier.

ACTIVITY - Antidiarrheic; Anti-HIV; Antibacterial. A total of 20 patients with traveler's diarrhea were entered into the study. Subjects were evaluated for the following parameters: (a) usual stool frequency (number of stools per day or week), (b) date and time of

diarrhea onset, (c) Number of stools in the past 24 hours, categorized according to consistency as follows: Formed: retains its original shape in water Soft: assumes shape of the container Watery: can be poured (stools of mixed form (e.g. soft/watery) were classified in the least formed category (e.g. watery)), (d) Symptoms experienced during the past 24 hours, including: cramping anal irritation tenesmus urgency (inability to delay timing by as long as 15 minutes) fecal incontinence (decreased control of bowel movements) inconvenience (interference with normal activities) nausea vomiting increased intestinal gas. After completion of the screening evaluations, samples for the baseline laboratory tests were obtained and the first dose of study medication was administered. The subjects were administered an initial loading dose of 1250 mg of the enteric coated proanthocyanidin polymer composition with three more doses of 250 mg every six hours for the first 24 hours of treatment, and then 500 mg four times per day for a total of 2 g per day on the second day of dosage. The proanthocyanidin polymer composition was only administered for two days. Results showed that the abnormal stool frequency trended toward normal over the three days of the study. The average number of stools per day returned to near-normal frequency by day 3. 4 patients returned to their normal stool frequency by the third study day. In addition, the time-to-last-unformed-stool was 30.3 hours on average.

MECHANISM OF ACTION - None given.

USE - The method is useful for treating secretory diarrhea in animals. The secretory diarrhea is caused by a bacterium or non-infectious etiology. The non-infectious etiology is chosen from non-specific diarrhea, ulcerative colitis and irritable bowel syndrome. The human suffering from secretory diarrhea is an infant or a child. The human is treated for HIV-associated chronic diarrhea. The human is treated for diarrhea caused by cholera. The non-human animal is treated for secretory diarrhea (all claimed).

ADVANTAGE - The formulation is enteric coated.

TECH BIOLOGY - Preferred Microorganism: The Croton sp is Croton lechleri. PHARMACEUTICALS - Preferred Components: The aqueous soluble proanthocyanidin polymer composition is coated with an enteric coating. The aqueous soluble proanthocyanidin polymer composition is formulated to protect the aqueous soluble proanthocyanidin polymer composition from the acidic conditions of the stomach in a controlled release preparation, and a carrier. The pharmaceutical composition is formulated as a compressed tablet. The pharmaceutical composition further comprises a lubricant. The lubricant is magnesium stearate. The pharmaceutical composition is formulated as an enteric coated capsule. The capsule contains beads comprising a core of the proanthocyanidin polymer composition and a layer of the enteric coating. The enteric coating is comprised of a methacrylic

acid-methacrylic acid ester copolymer with acid ionizable groups.

ABEX ADMINISTRATION - The pharmaceutical composition is administered orally (in animal feed), at a dose of 0.1-100 mg/kg/day, preferably 0.1-40 mg/kg/day of the aqueous soluble proanthocyanidin polymer composition (claimed). The pharmaceutical composition is administered in combination with protease inhibitors e.g. aprotin, and compounds that inhibit secretion of stomach e.g. ranitidine, nizatidine, famotidine, cimetidine and misoprostol.

EXAMPLE - Proanthocyanidin polymer composition (in mg) (250) is granulated with cross-linked sodium carboxymethylcellulose ('AC-DI-SOL.TM.') (7) and microcrystalline cellulose ('AVICEL.TM. PH 200/300') (sufficient mass) to bring the total mass to 350 mg. The ingredients were mixed for 20-30 minutes in a V blender. After the 20-30 minutes of mixing, 1.75 mg magnesium stearate was added and the mixture was blended for an additional 4-5 minutes. The resulting granules were compressed on a rotary tablet press using 5/16th inch standard concave punches. The tablets were coated with an enteric coating mixture prepared from Eudragit (RTM: acrylic resins comprising copolymers of acrylic and methacrylic esters with a low content of quarternary ammonium groups) L 30 D-55 (250 g), triethyl citrate (7.5 g), talc (37.5 g) and water (205 g). The tablets were then placed in a perforated pan coater and rotated at 15 rpm at 40degrees C. The enteric coating formulation was sprayed using the following conditions: inlet air temperature of 44-48degrees C, exhaust air temperature of 29-32degrees C, product temperature of 26-30degrees C, a 1 mm spray nozzle, a pan speed of 30-32 rpm, an airflow of 30-32 CFM, and a spray pressure of 20 PSI. The tablets were finally cured for 30 minutes as the pan is rotating at 15 rpm with an inlet air temperature of 60degrees C. and then, after shutting off the heat, the tablets were rotated at 15 rpm until the tablets have cooled to room temperature, to obtain 350 mg tablet.

L172 ANSWER 2 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2004-748581 [73] WPIX Full-text
ED 20050707
DNC C2004-263061 [73]
DNN N2004-591429 [73]
TI Manufacture of tablet of e.g. trandolapril, by suspending fine drug powder in insoluble liquid medium, spraying on additives, fluidized bed granulating and compression-molding to produce preset drug content after drying
DC B07; P33
IN TANIGUCHI T; TERAI T
PA (OHAR-N) OHARA CHEM IND LTD

CYC 101
PI WO 2004089344 A1 20041021 (200473)* JA 14[0]
AU 2003236336 A1 20041101 (200506) EN
JP 2004570538 X 20060706 (200645) JA 10
ADT WO 2004089344 A1 WO 2003-JP4193 20030401; AU 2003236336 A1 AU 2003-236336 20030401; AU 2003236336 A1 WO 2003-JP4193 20030401; JP 2004570538 X WO 2003-JP4193 20030401; JP 2004570538 X JP 2004-570538 20030401
FDT AU 2003236336 A1 Based on WO 2004089344 A; JP 2004570538 X Based on WO 2004089344 A
PRAI WO 2003-JP4193 20030401
IPCI A61K0038-55 [I,A]; A61K0009-20 [I,A]; A61P0043-00 [I,A]; A61P0009-00 [I,C]; A61P0009-12 [I,A]
IPCR A61K0009-20 [I,A]; A61K0009-20 [I,C]; A61P0009-00 [I,C]; A61P0009-12 [I,A]
EPC A61K0009-20H4B; A61K0009-20P
AB WO 2004089344 A1 UPAB: 20050707
NOVELTY - Tablet having uniform drug content is produced by uniformly suspending a fine powder-like drug having an average particle size of 1-20 mum in a insoluble liquid medium, spraying the obtained suspension on additive(s) under fluidization for fluidized bed granulation, and then compression-molding the grains to produce drug content of 0.1-10 wt.% (based on the whole tablet) after drying.
USE - For manufacturing tablet-having uniformity of drug (such as trandolapril, perindopril, etizoram or butyzoram) content.
ADVANTAGE - Tablet having uniformity of content and high storage stability can be manufactured advantageously in short time, industrially without increasing processing steps. The deactivation of medicaments during tablet manufacture is suppressed.
TECH ORGANIC CHEMISTRY - Preferred Component: The suspension contains a binder. The liquid medium is water. Preferred Amount: The suspension and formulation contain 1-15 wt.% of the binder. The content of binder is 100-1000 wt.% with respect to medicaments.
ABEX EXAMPLE - Lactose (3195 g), polyvinyl pyrrolidone (90 g) and partially (alpha)-lyzed starch (150 g) were mixed, supplied to fluidized bed granulator and fluid bed was formed. Suspension was formed by dispersing trandolapril powder (30 g) having average particle diameter of 8 mum in solution containing pure water (690 ml) and polyvinyl pyrrolidone (60 g). The liquid was sprayed in the fluid bed at a velocity of 40 g/minute. The temperature and airflow were controlled, such that air taken into the granulator was set to 60degreesC and exhaust gas temperature was 25-30degreesC. 5 minutes ventilation drying was performed after spraying was completed and granulated substance was obtained. The granulated substance was sieved using JIS standard sieve of 24 meshes, and particle size regulated powder was obtained. Hardened oil (75 g) was added to the particle size regulated powder, mixed

uniformly, compression-molded by rotary tabletting machine and tablets were produced. Each tablet (120 mg) contained trandolapril (1 mg), lactose (106.5 mg), polyvinyl pyrrolidone (5 mg), partially (alpha)-lyzed starch (5 mg) and hardened oil (2.5 mg). The tablets were sealed-preserved or opened-preserved in petri-dish at 60degreesC and 75% humidity. The residual amount of medicament of each tablet was measured by high performance liquid chromatography after 10 days. The residual amount of medicament was 97% in closed petri-dish-preserved tablet and 95.7% in open petri-dish-preserved tablet. The tablets were also tested for uniformity of content as described in 14th edition, Japanese Pharmacopoeia. The results showed that the tablet had compatible uniformity of content.

L172 ANSWER 3 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2004-718729 [70] WPIX Full-text
ED 20050707
DNC C2004-253231 [70]
DNN N2004-569791 [70]
TI Dry powder inhalation system for treating respiratory disease e.g. asthma, comprises micronized active ingredient in hydroxypropylmethylcellulose container and dry powder inhaler device equipped with piercing systems
DC A96; B05; B07; P34
IN BAUDIER P; DEBOECK A; VANDERBIST F; BAUDUER P
PA (GALE-N) GALEPHAR M/F; (BAUD-I) BAUDUER P; (DEBO-I) DEBOECK A
CYC 107
PI WO 2004082750 A1 20040930 (200470)* EN 43[10]
EP 1603615 A1 20051214 (200582) EN
US 20060254583 A1 20061116 (200677) EN
EP 1603615 B1 20080709 (200847) EN
ADT WO 2004082750 A1 WO 2004-BE39 20040317; EP 1603615 A1 EP 2004-721094 20040317; EP 1603615 A1 WO 2004-BE39 20040317; US 20060254583 A1 WO 2004-BE39 20040317; US 20060254583 A1 US 2006-549124 20060619; EP 1603615 B1 EP 2004-721094 20040317; EP 1603615 B1 WO 2004-BE39 20040317
FDT EP 1603615 A1 Based on WO 2004082750 A; EP 1603615 B1 Based on WO 2004082750 A
PRAI WO 2003-BE48 20030320
IPCI A61M0015-00 [I,A]; A61M0015-00 [I,C]; A61M0015-00 [I,C]; A61M0016-10 [I,A]; A61M0016-10 [I,C]
IPCR A61K0009-00 [I,A]; A61K0009-00 [I,C]; A61M0015-00 [I,A]; A61M0015-00 [I,C]
EPC A61K0009-00M20B3; A61M0015-00C
ICO K61M0015:00C1P; K61M0202:06B
NCL NCLM 128/203.150
NCLS 128/203.120; 128/203.210

AB WO 2004082750 A1 UPAB: 20060203

NOVELTY - A dry powder inhalation system (S1) comprises at least one micronized active ingredient (a1), optionally in association with excipients, contained in a hydroxypropylmethylcellulose container (c1) having an outer surface extending between two end portions intended to be pierced or perfored, and dry powder inhaler device (b1) equipped with at least two substantially identical piercing systems (s1).

DETAILED DESCRIPTION - A dry powder inhalation system (S1) comprises at least one (preferably at least two) micronized active ingredient (a1), optionally in association with excipients, contained in a hydroxypropylmethylcellulose container (c1)(preferably capsule) optionally elongated having an outer surface optionally elongated with a longitudinal axis of symmetry, extending between two optionally curved end portions intended to be pierced or perfored, and dry powder inhaler device (b1) equipped with at least two substantially identical piercing systems (s1), able to pierce or perfore (c1) at the two end portions. (s1) have an equivalent diameter of not less than 0.8 (preferably not less than 1) mm. (s1) are adapted so that the equivalent diameter of the hole(s) pierced by each piercing system after removal of the piercing system from the hole(s) is 10 - 31 or 9 - 30 (preferably 15 - 26 or 14 - 25) % of the equivalent diameter of the cross section of the portion of the outer surface of (c1) to be pierced located between the two pierced end portions. The cross section is located in a plane perpendicular to an axis extending between the end portions (preferably a symmetrical axis extending between the end portions).

ACTIVITY - Respiratory-Gen.; Antiasthmatic.

MECHANISM OF ACTION - None given.

USE - For treating respiratory disease or preventing respiratory troubles for administering at least one ingredient in the lungs or in the systemic circulation (claimed). The respiratory disease includes asthma.

ADVANTAGE - The system provides high respiratory dose of the active ingredient thus increasing the lung deposition of the drug.

TECH INSTRUMENTATION AND TESTING - Preferred System: (s1) are bevel-edged needles or pins. The number of (s1) per device is less than 8 (preferably less than 5, especially less than 3). (a1) is mixed with carrier before being filled in (c1). (S1) with two (s1) comprising each a single pin, the inhalation system is composed of at least one bucal piece and one basal piece adapted for containing (c1) or capsule. The basal piece is equipped with (s1) and at least one pressing button for operating the pins of (s1).

PHARMACEUTICALS - Preferred Components: The carrier is a mono- or disaccharide derivative (preferably lactose). The mean size of (a1) is less than 10 (preferably less than 8, especially less than 6) mum. (a1) is from the class of mucolytic, bronchodilator,

corticosteroid, xanthine derivative, leukotriene antagonist, proteins and/or peptide (preferably L-lysine N-acetylcysteinate).

ABEX ADMINISTRATION - The capsule containing a therapeutically active agent is partly broken and administered by inhalation (claimed).

EXAMPLE - Micronized formoterol fumarate was formulated in dry powder inhaler (DPI) (0.012 mg/capsule) and then the powder was filled into either hard gelatin capsules or hydroxypropylmethylcellulose (HPMC) capsules. The average particle size of the formoterol containing powder was about 3 mum. The in-vitro deposition tests were performed. A fine particle dose (FPD) of formoterol obtained from each type of capsule was (mug) 2.63 +/- 0.16 and 2.24 +/- 0.12 for hard gelatin capsules and HPMC capsules respectively. When a given DPI formulation fumarate of formoterol was filled in respectively hard gelatin capsules or HPMC capsules and administered with the four pin device, the FPD which was representative of the in vitro lung deposition was higher for the powder filled into hard gelatin capsules than in HPMC capsules. The HPMC capsules had some potential advantages over hard gelatin capsules, which made them theoretically more performant than the hard gelatin capsules for administering DPI formulations. But the results showed the superiority to hard gelatin capsules. The holes made in hard gelatin capsules were significantly larger than the holes made in HPMC capsules. The shape of the holes perforated in HPMC capsules was more regular than the shape of the holes perforated in hard gelatin capsules. The four pin device equipped with pins of a diameter of 0.6+/-0.1 mm, the holes were smaller but presenting a more regular shape with HPMC capsules than with hard gelatin capsules, resulted in a lower FPD value for HPMC capsules. The same hard gelatin and HPMC capsules containing the same formoterol fumarate formulation were again tested but this time, they were administered using the single pin device. The FPD obtained was (mug) 2.67 +/- 0.12 (for hard gelatin capsules) and 3.25 +/- 0.2 (for HPMC capsules). The FPD obtained from HPMC capsules + single pin device was higher than those obtained with hard gelatin capsules+single pin device. The results obtained with the combination HPMC capsules+single pin device were significantly higher than the results obtained with HPMC capsules+four pin device. The conclusion of this experiment was that the combination described in the present invention i.e. HPMC capsules+single pin DPI devices allowed to obtain an higher FPD value and hence the highest in vitro lung deposition. Neither the HPMC capsules alone, nor the single pin device alone was sufficient to provide this high lung deposition. Only the combination of both parameters to form an integrated inhalation system allowed improving the lung deposition of the drug.

L172 ANSWER 4 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2004-661862 [64] WPIX Full-text
ED 20050531
DNC C2004-236312 [64]
TI Transmucosal delivery composition comprises an ionizable pharmaceutical agent (e.g. antihypertensive agent and analgesic) and one or more complementary lipophilic species
DC A96; B05; B07
IN MCCARTY J A
PA (PHAR-N) THARM PRODN INC; (MCCA-I) MCCARTY J A
CYC 107
PI WO 2004075877 A1 20040910 (200464)* EN 68[6]
AU 2004216098 A1 20040910 (200565) EN
AU 2004216098 A2 20040910 (200570) EN
EP 1599186 A1 20051130 (200578) EN
MX 2005008918 A1 20060201 (200643) ES
KR 2005120753 A 20051223 (200652) KO
JP 2006518761 W 20060817 (200654) JA 51
CN 1777411 A 20060524 (200663) ZH
IN 2005KN01624 P2 20070105 (200725) EN
US 20070071806 A1 20070329 (200725) EN
ADT WO 2004075877 A1 WO 2004-US5490 20040224; AU 2004216098 A1 AU 2004-216098 20040224; AU 2004216098 A2 AU 2004-216098 20040224; CN 1777411 A CN 2004-80010600 20040224; EP 1599186 A1 EP 2004-714139 20040224; EP 1599186 A1 WO 2004-US5490 20040224; MX 2005008918 A1 WO 2004-US5490 20040224; KR 2005120753 A WO 2004-US5490 20040224; JP 2006518761 W WO 2004-US5490 20040224; MX 2005008918 A1 MX 2005-8918 20050822; KR 2005120753 A KR 2005-715592 20050823; JP 2006518761 W JP 2006-503842 20040224; US 20070071806 A1 Provisional US 2003-449647P 20030224; US 20070071806 A1 WO 2004-US5490 20040224; IN 2005KN01624 P2 WO 2004-US5490 20040224; IN 2005KN01624 P2 IN 2005-KN1624 20050816; US 20070071806 A1 US 2006-545774 20060808
FDT AU 2004216098 A1 Based on WO 2004075877 A; AU 2004216098 A2 Based on WO 2004075877 A; EP 1599186 A1 Based on WO 2004075877 A; MX 2005008918 A1 Based on WO 2004075877 A; KR 2005120753 A Based on WO 2004075877 A; JP 2006518761 W Based on WO 2004075877 A
PRAI US 2003-449647P 20030224
US 2006-545774 20060808
IC ICM A61K009-00
AB WO 2004075877 A1 UPAB: 20060203
NOVELTY - Composition (A) comprises an ionizable pharmaceutical agent (1) and one or more complementary lipophilic species (2) formulated in a transmucosal dosage form.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method for transmucosal delivery of (1) comprising admixing (1) with one or more complementary (2) to form a lipophilic association (LA), formulating the LA in a transmucosal dosage form and administering the transmucosal dosage form to a targeted mucosal membrane in order to deliver (1) through the mucosal membrane and into systemic circulation.

ACTIVITY - Hypotensive; analgesic; antidepressant; anesthetic; antiarrhythmic; antiarthritic; antispasmodic; respiratory-gen.; antianginal; uropathic; antidiabetic; hypertensive; antiparkinsonian; cytostatic; immunosuppressive; antiemetic; antibacterial; fungicide; virucide; antimuscarinic; antiallergic; tranquilizer; sedative; neuroleptic; osteopathic; cardioactive; antilipemic; antimalarial; anticonvulsant; antihelminthic; antismoking; antitussive; gastrointestinal-gen.; muscle relaxant; anorectic; antithyroid; antimigraine.

MECHANISM OF ACTION - Angiotensin-converting-enzyme-inhibitor; opioid agonist.

USE - (A) is useful for transmucosal delivery of (1) (claimed). No biological data given.

TECH PHARMACEUTICALS - Preferred Composition: (1) is hydrogen-bonded or ion-paired to (2) forming a lipophilic association (LA). (A) further comprises a solvent (ethanol, ethyl acetate, isopropyl alcohol, triacetin, triethyl citrate, tributyl citrate, a polyethylene glycol, propylene glycol, bisabolol, glycerin, mineral oil, ethyl oleate, a fatty acid ester, squalane, an animal oil, a vegetable oil, a hydrogenated vegetable oil, isopropyl myristate, isopropyl palmitate, glycofurol, a terpene, an essential oil, an alcohol, a polyol, a silicone fluid or a glyceride) having a dielectric constant less than that of water (where the LA is solvated in the solvent to form a solubilized LA), a carrier (a silica or a silicified microcrystalline cellulose) (where the LA is adsorbed or absorbed to the carrier), a water-soluble excipient (sugar, polyol, alcohol, saccharide, polysaccharide, glycerin, propylene glycol, ethanol, isopropyl alcohol, ethyl acetate, triacetin, triethyl citrate, tributyl citrate, a dextrate, dextrin, dextrose, fructose, lactitol, lactose, erythritol, maltose, maltitol, maltodextrin, polydextrose, trehalose, mannitol, polyethylene glycol, sorbitol, sucrose or xylitol) possessing a dielectric constant less than the dielectric constant of water, a buffering agent (phosphate, carbonate, tartrate, borate, citrate, acetate or maleate), colorant, flavoring, solvent, co-solvent, coating agent, binder, diluent, carrier, disintegrant, glident, lubricant, opacifying agent, humectant, granulating agent, gelling agent, polishing agent, suspending agent, sweetening agent, anti-adherent, preservative, emulsifying agent, antioxidant, levigating agent, plasticizer, surfactant, tonicity

agent, viscosity agent, enteric agent, enteric coating, controlled-release agent or coating, wax, wetting agent, thickening agent, suppository base, stiffing agent, stabilizing agent, solubilizing agent, sequestering agent, ointment base, oleaginous vehicle, film-forming agent, essential oil, emollient, dissolution enhancer, dispersing agent and/or cryoprotectant. The carrier is capable of forming an inclusion complex with the LA or solubilized LA. The molar ratio of (2) to (1) is at least about 1:1. (1) possesses an acidic or a basic functional group and (2) is an acid (i) (fatty acid, a long-chain alkyl sulfonic acid or a long-chain alkyl sulfuric acid) or a base (preferably cetrimide, oleamidopropyl dimethylamine, didecyldimethyl ammonium chloride, a quaternary surfactant, cetylpyridinium chloride, hexetidine, benzalkonium chloride or an amine or amide of (i)). (1) is dihydroergotamine, fentanyl, sufentanil, lidocaine, alfentanil, lofentanil, carfentanil, pentobarbital, buspirone, ergotamine, bisphosphonate, alendronic acid, nalbuphine, bupropion, metformin, diethylcarbamazine, tramadol, heparin or a heparin derivative, amoxicillin, gabapentin, econazole, aspirin, prostaglandin, methylsergide, ergonovine, endorphins, enkephalins, oxytocin, opiates, heparin and its derivatives, clorazepic acid, barbiturate, albuterol, atropine, scopolamine, selegiline, timolol, nicotine (preferred), cocaine, novocaine, amphetamines, caffeine, methylphenidate, chlorpromazine, ketamine, epinephrine, estropipate, naloxone, naltrexone, furosemide, labetalol, metoprolol, nadolol, isoproterenol, terbutaline, sumatriptan, bupivacaine, prilocaine, loratadine, chloropheniramine, clonidine or tetracaine. (1) is a antihypertensive agent, analgesic, antidepressant, opioid agonist, anesthetic, antiarrhythmic, antiarthritic, antispasmodic, ACE inhibitor, decongestant, antibiotic, antihistamine, anti-anginal, diuretic, anti-hypotensive agent, anti-Parkinson agent, bronchodilator, oxytocic agent, anti-diuretic, anti-hyperglycemic, antineoplastic and/or immunosuppresent agent, antiemetic, antiinfective, antifungal, antiviral, antimuscarinic, antidiabetic agent, antiallergy agent, anxiolytic, sedative, antipsychotic, bone modulating agent, cardiovascular agent, cholesterol lowering drug, antimalarial, antiepileptic, antihelminthic, agent for smoking cessation, cough suppressant, expectorant, mucolytic, nasal decongestant, dopaminergic, gastrointestinal agent, muscle relaxant, neuromuscular blocker, parasympathomimetic, prostaglandin, stimulant, anorectic, thyroid or antithyroid agent, hormone, antimigraine agent, antiobesity and/or non-steroidal anti-inflammatory agent. (A) is prepared as a buccal tablet, sublingual tablet, oral capsule, oral tablet, nasal spray, buccal or vaginal spray, liquid/semisolid, aerosol for nasal, buccal or pulmonary delivery, patch, lozenge, gum, lollypop, film, strip, paper, suppository or pessary dosage form. (A), when dissolved in

water, has a pH of about or near the physiological pH of a target mucosal membrane.
Preferred Method: Admixing (1) with (2) is performed under conditions such that (1) hydrogen-bonds or ion-pairs with (2). The method further comprising solubilizing the LA with a solvent having a dielectric constant less than that of water to form a solubilized LA. (1) is delivered rapidly across the mucosal membrane (oral mucosa, esophagus, gastrointestinal tract, lungs, rectum, sinuses, eye, urinary tract or a lining of a female reproductive organ) in about 10 minutes or less. The dosage form is manufactured by direct tablet compression, wet or dry granulation, dry powder blends, molding, spray-congealing, powder layering, tableting, encapsulating, spray-drying, spheronization, triturates, lyophilization, freeze drying, co-melt, microencapsulation, troching, pelleting, aerosolizing, liquid or semisolid processes. The nicotine is transmucosally delivered sublingually at a pH between 5.5 and 7.5.

ABEX ADMINISTRATION - Administration of (A) is oral, sublingual, buccal, vaginal, rectal, pulmonary, ophthalmical or intranasal.
SPECIFIC COMPOUNDS - The use of caproic acid, caprylic acid, capric acid, lauric acid, myristic acid, palmitic acid, stearic acid, arachidic acid, behenic acid, lignoceric acid, myristoleic acid, palmitoleic acid, oleic acid, gadoleic acid, erucic acid, ricinoleic acid, linoleic acid, linolenic acid, licanic acid, arachidonic acid and clupanadonic acid is specifically claimed as (2).

L172 ANSWER 5 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2004-487576 [46] WPIX Full-text
ED 20050530
DNC C2004-181662 [46]
TI Obtaining cellulosic wet sheet used e.g. as thickening agent in food and beverage industry, comprises heating solution containing glucose mass and yeast extract in water, adding inoculum Acetobacter xylinum, and fermenting in covered trays
DC A97; B04; D13; D16; F09; J01; J04; P34
IN FERREIRA LEVY N L; KUROKAWA E C; LEVY N L F; PODLECH P A S; SANCHEZ PODLECH P A
PA (LEVY-I) FERREIRA LEVY N L; (LEVY-I) LEVY N L F; (KURO-I) KUROKAWA E C; (PODL-I) PODLECH P A S
CYC 106
PI WO 2004050986 A1 20040617 (200446)* EN 30[14]
BR 2002005499 A 20040803 (200454) PT
AU 2003283089 A1 20040623 (200472) EN
EP 1570124 A1 20050907 (200559) EN
US 20060134758 A1 20060622 (200642) EN
ADT WO 2004050986 A1 WO 2003-BR174 20031126; BR 2002005499 A BR 2002-5499 20021205; AU 2003283089 A1 AU 2003-283089

20031126; EP 1570124 A1 EP 2003-773361 20031126; EP 1570124 A1 WO 2003-BR174 20031126; US 20060134758 A1 WO 2003-BR174 20031126; US 20060134758 A1 US 2006-538131 20060130

FDT AU 2003283089 A1 Based on WO 2004050986 A; EP 1570124 A1 Based on WO 2004050986 A

PRAI BR 2002-5499 20021205

IPCI C12P0019-00 [I,C]; C12P0019-04 [I,A]

IPCR B01D0069-00 [I,C]; B01D0069-06 [I,A]; B01D0071-00 [I,C]; B01D0071-10 [I,A]; C12P0019-00 [I,C]; C12P0019-04 [I,A]; D21C0005-00 [I,A]; D21C0005-00 [I,C]

EPC B01D0069-06; B01D0071-10; C12P0019-04; D21C0005-00

NCL NCLM 435/101.000

AB WO 2004050986 A1 UPAB: 20060121

NOVELTY - Cellulosic wet sheet is obtained by heating a solution containing 0.2-12% glucose mass and 0.1-7% yeast extract in water at 125degreesC for 15 minutes; cooling the solution till it reaches 5-30degreesC; adding 0.5-5% ethanol and 2-50% inoculum Acetobacter xylinum; transferring the solution to covered fermentation trays where it must rest for 16-240 hours, at 5-30degreesC; and collecting the formed cellulose wet sheets.

DETAILED DESCRIPTION - Obtaining cellulosic wet sheet comprises: (a) heating a solution containing 0.2-12% glucose mass and 0.1-7% yeast extract in water that was filtered through sand and activated charcoal, in a sanitary stainless steel mixer with a steam heated jacket, at 125degreesC for 15 minutes, for sterilization purposes; (b) cooling the solution till it reaches 5-30degreesC; (c) adding 0.5-5% ethanol and 2-50% inoculum Acetobacter xylinum followed by agitation of the solution until it is homogenized; (d) transferring the solution to covered fermentation trays where it must rest for 16-240 hours, at 5-30degreesC; (e) collecting the cellulose wet sheets that are thus formed, varying 0.25-200 mm in thickness; (f) forwarding the wet sheets to the whirlpool tank, where they are purified and whitened, according to the following sequence: rinsing, washing with sodium hydroxide 1-5%, rinsing, washing with 1-5% sodium lauryl sulfate and final rinsing; and (g) packaging the wet sheets for shipping.

INDEPENDENT CLAIMS are also included for the following:

(1) process used to obtain cellulosic membrane from wet sheet, comprising (h) in one of the extremities of the wet sheet, applying by pressure two rectangles of an absorbent material; (i) inserting this extremity in the drying equipment through an idling roller, introducing between two pairs of draining cylinders, pressing between pair of conveyor belts with increasing force (from 0.5-8 kgf/cm2) that is applied by a series of small rollers heated by the hot water that circulates in their axles, passing through a pair of finishing cylinders; and (j) forwarding the formed membrane to a coiling

device, where the product is coiled and stands ready for sterilization and/or shipping;

(2) culture medium comprising containing filtered water, 0.2-12% glucose mass, 0.1-7% yeast extract, and 0.5-5% ethanol;

(3) fermentation tray comprising tray with a double wall and a covering made of non-adherent material, preferably fiberglass with reinforced structure, where the tray walls are 2-3 mm thick and form a duct where water circulates to keep the temperature at ideal point for fermentation;

(4) equipment for obtaining the membrane, comprising a black steel plate structure of appropriate thickness, forming a box with a lid that is normally closed and, for the purpose of ensuring the operator's safety, with a power switch that arrests the motor when the lid is not totally shut, and an idling roller coated with an absorbent material; two pairs of draining cylinders made of stainless steel coated with an absorbent material, 20 cm in diameter and 30 cm in width, where the upper cylinder of the first pair is provided with a foot-actuated lifting mechanism and a lever system designed to permit the initial positioning of the wet sheet between the two cylinders; two pairs of stainless steel driving cylinders, 20 cm in diameter and 30 cm in width, with roller bearings, where the cylinders numbered are not powered and the cylinders numbered are powered with a speed of 15-60 rpm; two felt (or any other water absorbing material) continuous conveyor belts measuring 2 m by 30 cm that are moved by the cylinders, and two rollers to control the tension on the belts, also made of stainless steel, with 10 cm in diameter; twelve or more pairs of stainless steel rollers, their external diameters measuring 5 cm each, the bottom ones heated by the passing of hot water or vapor through their axles, each pair of rollers making it possible to apply increasing pressure to the conveyor belts made of absorbent material; pair of finishing cylinders made of polished stainless steel, 20 cm in diameter and 30 cm long, each exerting pressure on the other, that can be heated by inner circulation of steam or hot water; and a coiling device (10) made of carbon steel; and

(5) cellulosic membrane composed of pure cellulose microfibrils produced by microorganisms, randomly arranged, with an ideal weight of 10-45 g/m2, and being membrane permeable to gases and impermeable to liquids.

USE - The process is used for obtaining cellulosic wet sheet used as thickening and/or stabilizer in the food and beverage industry such as in nonfat milk, juices and food; used in the making of artifacts obtained by drying and shaping the wet sheets (compound and not compound alike) in the forms desired for the final product, either pressed or non-pressed; included in the composition of canned foods; used in the production of sweets; and used to obtain extremely thin cellulosic membranes with characteristic properties such as

permeability to gases and impermeability to liquids. It can also be used in the production of lightweight plates extremely resistant to impact and bullet perforations. It may also be used in hospital and surgical applications. It is used to obtain cellulosic membranes that are used as a device to obtain an environment suitable for in vivo culture in the regeneration of tissues in living organisms, both externally and internally, due to their biocompatibility that prevents rejection; as a temporary substitute for the skin, mainly in dermal ulcers, burns, recovery of autograft-donor sites, membrane for ophthalmic use, odontological use, dressings for home use, professional use, veterinary use; as functional material in the making of hospital attire and disposable packaging for medical and nursing instruments whenever a microbial barrier is recommended, and also as thickener to replace sugar, starch, carboxymethylcellulose, and microcrystalline cellulose in the making of medicine tablets; as engineering and safety material, specially as a bulletproof material; and as diaphragm in the production of speakers and earphones (all claimed).

ADVANTAGE - The process obtains wet sheet of high purity and specific physical and chemical properties in industrial scale. It avoids the need for humidity control, avoid the need for forced air circulation, does not form lamella in the zooglea thus preventing waste of material and labor to pull it off, and avoids the need to stretch the wet sheets on stenters to dry or its freezing. It is more economical and yields better results, and assures consistent quality.

DESCRIPTION OF DRAWINGS - The figure shows a flow chart of the process used to obtain cellulosic wet sheet and membrane from wet sheet.

TECH POLYMERS - Preferred Process: The process optionally comprises adding screens or other artifacts of diverse materials to the surface of the wet sheet already pre-formed; resting for 16 -240 hours at 5-30degreesC; and collecting of the compound cellulose wet sheets having a thickness 0.25-40 mm. All effluents are recovered and treated before they are reused or disposed of in the sewer system. The wet sheet may be processed in blenders or mills, resulting in a thick mass with a great power to retain liquids. Preferred Product: The obtained wet sheet is made of randomly arranged pure cellulose microfibrils with a great capacity to retain liquids, keeping the humidity retained in its structure in excess of 90%. It is cartilage-like and of a whitish color. It resists high temperatures and optionally may be submitted to autoclave treatment in liquid medium under high temperature and pressure without suffering any physical changes. It is insoluble in organic solvents.

L172 ANSWER 6 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2004-110791 [12] WPIX Full-text
ED 20050528

DNC C2004-045142 [12]
TI Production of effervescing tablets involves first forming an acid/polyol pre- mix before mixing in the other ingredients and then tabletting
DC B07; D13
IN DANI J; MEYER F; SCHNEIDER A
PA (KRUE-N) KRUEGER GMBH & CO KG
CYC 1
PI DE 10230588 A1 20040115 (200412)* DE 5[0]
ADT DE 10230588 A1 DE 2002-10230588 20020705
PRAI DE 2002-10230588 20020705
IPCR A23L0001-236 [I,A]; A23L0001-236 [I,C]; A23L0001-302 [I,A]; A23L0001-302 [I,C]; A23L0001-304 [I,A]; A23L0001-304 [I,C]; A61K0009-46 [I,A]; A61K0009-46 [I,C]
EPC A23L0001-236; A23L0001-236D2; A23L0001-302; A23L0001-304; A61K0009-00L6
AB DE 10230588 A1 UPAB: 20050528
NOVELTY - Production of effervescing tablets comprises
(1) premixing a conventional acid and a liquid polyol;
(2) mixing with active agent(s), a conventional carbonate and optionally other ingredients; and
(3) directly pressing the mixture.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a pre-mix comprising a conventional solid acid, especially citric acid, at 97-99.7 wt.% and propyleneglycol and/or glycerol at 0.3-3 wt.%.
USE - E.g. in foods, nutritional supplements, medicines, disinfectants, descaling agents or detergents.
ADVANTAGE - The mixture thus obtained has improved tabletting properties.
TECH ORGANIC CHEMISTRY - Preferred Process : In the manufacture of the pre- mix the polyol is sprayed on the acid. Steps (2) and (3) are carried out in an air- conditioned space.
Preferred Composition The tablets contain the polyol at 0.01-1 wt.%.
ABEX EXAMPLE - Tablets with a 500 mg calcium content per 4.5 g tablet comprise (per 100 g) calcium carbonate (27.778 g), citric acid (53.356 g), sodium bicarbonate (9 g), citric acid/propyleneglycol mixture (5 g; i.e. 50 mg propylene glycol), fructose (2.000 g), cyclamate/saccharine (1.760 g), aromas (1.100 g) and dyes (0.006 g).

L172 ANSWER 7 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2003-731396 [69] WPIX Full-text
ED 20050601
DNC C2003-201221 [69]
TI Pharmaceutical composition used for sustained release delivery of therapeutically active group comprises tablet core surrounded by release rate controlling membrane

DC A96; B05; B07
IN DEB J K; GARG S; GOUTAM K; KAUL C L; SRIVASTAVA P; VERMA R K; CHAMAN L; KUMAR K; VERMA R
PA (COUL-C) COUNCIL SCI & IND RES; (COUN-N) COUNCIL SCI & IND RES INDIA; (INTE-N) INDIAN INST TECHNOLOGY
CYC 99
PI WO 2003063825 A1 20030807 (200369)* EN 27[9]
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US 20030175349 A1 20030918 (200369) EN
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AU 2002244905 A1 20030902 (200422) EN
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EP 1469824 A1 20041027 (200471) EN
KR 2004091006 A 20041027 (200516) KO
CN 1622799 A 20050601 (200560) ZH
DE 60206078 E 20051013 (200568) DE
JP 2006508891 W 20060316 (200620) JA 35
ES 2248529 T3 20060316 (200622) ES
ZA 2004006112 A 20060628 (200648) EN 68
ADT WO 2003063825 A1 WO 2002-IN62 20020322; US 20030175349 A1 US 2002-101237 20020320; AU 2002244905 A1 AU 2002-244905 20020322; CN 1622799 A CN 2002-828669 20020322; DE 60206078 E DE 2002-606078 20020322; EP 1469824 A1 EP 2002-713167 20020322; DE 60206078 E EP 2002-713167 20020322; ES 2248529 T3 EP 2002-713167 20020322; EP 1469824 A1 WO 2002-IN62 20020322; DE 60206078 E WO 2002-IN62 20020322; JP 2006508891 W WO 2002-IN62 20020322; JP 2006508891 W JP 2003-563519 20020322; KR 2004091006 A KR 2004-712012 20040730; ZA 2004006112 A ZA 2004-6112 20040730
FDT DE 60206078 E Based on EP 1469824 A; AU 2002244905 A1 Based on WO 2003063825 A; EP 1469824 A1 Based on WO 2003063825 A; DE 60206078 E Based on WO 2003063825 A; JP 2006508891 W Based on WO 2003063825 A; ES 2248529 T3 Based on EP 1469824 A
PRAI IN 2001-DE96 20020130
IN 2001-DE96 20010130
AB WO 2003063825 A1 UPAB: 20060120
NOVELTY - Pharmaceutical composition comprises a tablet core surrounded by a release rate controlling membrane. The tablet core comprises an active group having limited solubility in aqueous fluids, an alkalinizing agent or a buffer compound and an osmotic solute. The release rate controlling membrane comprises a semipermeable membrane forming polymer, a permeable membrane forming polymer and at least one plasticizer.
DETAILED DESCRIPTION - Pharmaceutical composition comprises a tablet core surrounded by a release rate controlling membrane. The

tablet core comprises a therapeutically active group (a) having limited solubility in the aqueous fluids, weakly acidic and having a pKa of 2.5-7.5, an alkalinizing agent (b1) or a buffer compound (b2) in immediate contact with (a), an osmotic solute (c) that is soluble in water and capable of exhibiting an osmotic pressure gradient across the release rate controlling membrane against the external fluids, and optionally an excipient (d1) or polymer (d2).

The release rate controlling membrane comprises a semi-permeable membrane forming polymer (e) that is insoluble in water but partially permeable to aqueous fluids and impermeable to the core composition, a permeable membrane forming polymer (f) that is soluble in water and permeable to aqueous fluids, and to at least one of group of the core composition and 2-6 wt.% at least one plasticizer (g) based on the total weight of dry polymers.

An INDEPENDENT CLAIM is also included for the preparation of the pharmaceutical composition which comprises:

(1) preparing the core composition by:

(i) dry blending (a), (b1) or (b2), (c) and optionally one (d1) or (d2);

(ii) slugging or wet granulating by blending (a) with the other excipients including (b1) or (b2) and (c) using water, alcohol or an organic co-solvent (e.g. isopropyl alcohol/methylene chloride (80/20 vol./vol.)) as a granulation fluid to obtain wet granules, or

(iii) dissolving (a) and (b1) in a aqueous or organic solvent, evaporating to dryness and mixing the residue with (c) and other excipients, and

(2) compressing the formed core composition to obtain tablet cores using a conventional tablet making machine;

(3) preparing a coating solution by dissolving (e) in a solvent comprising methylene chloride, methanol and/or ethanol;

(4) adding (f) and at least one (g) to the solution with continuous stirring;

(5) coating the compressed tablet of step (2) with the coating solution of step (4) by press coating, spraying, dipping or air suspension technique, and

(6) drying the coated tablet core obtained in step (5) at 40-60degreesC for 16 hours to obtain the sustained release composition and packing the tablets by conventional methods.

ACTIVITY - Nootropic; Neuroprotective; CNS-Gen.; Muscular-Gen.; Cardiovascular-Gen.; Endocrine-Gen; Hemostatic; Immunosuppressive; Immunostimulant; Vasotropic; Gynecological; Antiallergic; Antiinflammatory; Antidiabetic; Sedative.

MECHANISM OF ACTION - None given.

USE - Used for sustained and extended release of active ingredient having limited solubility in aqueous fluids (claimed) and for treating a disease by using the active ingredient which is a drug that acts on peripheral nerves, nervous system, skeletal muscles,

cardiovascular system, smooth muscles, blood circulatory system, synaptic sites, neuroeffector junctional sites, endocrine and hormone system, immunological system, reproductive system, skeletal system,autocoid system, alimentary and excretory systems, inhibitory or autocoids and histamine systems, and material that act on the central nervous system e.g. hypnotics and sedatives.

ADVANTAGE - The pharmaceutical composition is used for extended delivery of a therapeutically active ingredient, limited solubility of which would preclude its incorporation into conventional osmotic compositions. The pharmaceutical composition is simple to manufacture and the solubility of the therapeutically active ingredient is improved, based upon their ability to modulate the micro environmental pH. The pharmaceutical composition does not require sophisticated techniques e.g. laser drilling across the membrane wall to form passageway(s) for the release of drug, and semipermeable and permeable polymers controls the release of the drug. The pharmaceutical composition requires minimum number of manufacturing steps and is simple in design and easily amenable to mass production.

TECH PHARMACEUTICALS - Preferred Composition: (e) and (f) together with (g) are coated on the tablet core and dried to obtain the release rate controlling polymer membrane. Each tablet contains 0.1-600 mg (a). The ratio of (a) and (b1) or (b2) is 0.1:9.9-7:3. The core components exert an osmotic gradient across the wall of the release rate controlling membrane against the external fluids. (e) is water insoluble and allows water to penetrate and prevents permeability of compositions of the tablet core. (f) is water soluble and allows water to penetrate along with at least one of the components of the core. The ratio of (e) to (f) is 9:1-1:9 (preferably 9:1-3:7). (g) has controlled solubility in water. The thickness of the release rate controlling membrane wall is controlled by adjusting the weight of the polymer forming membrane coated on the tablet. The coating solution on the tablet core is upto 20 wt.% of the core. The thickness of the membrane wall is 1-1000 (preferably 50-500) mum.

Preferred Components: (a) is a drug that acts on peripheral nerves, adrenergic receptors, cholinergic receptors, nervous system, skeletal muscles, cardiovascular, smooth muscles, blood circulatory system, synaptic sites, neuroeffector junctional sites, endocrine and hormone system, immunological system, reproductive system, skeletal system, autocoid systems, alimentary and excretory systems, inhibitory or autocoids and histamine systems, hypoglycemic agent, antiinflammatory agent (preferably sulfonylurea), or material that acts on the central nervous system selected from hypnotic or sedative (preferably acetazolamide, acetyl salicylic acid, para-amino salicylic acid, captropil, carbenicillin, carbenoxolone, chlorpropamide, clofibrate,

diclofenac, diflunisal, ethacrynic acid, etodolac, fenoprofen, furosemide, gliclazide, glimepiride, glipizide, glyburide, ibuprofen, indomethacin, ketoprofen, naproxen, nimesulide, tolazamide, tolbutamide, tolmentin, zomepirac, aspirin or paracetamol, especially gliclazide, glimepiride, glipizide, glyburide, ibuprofen, indomethacin, ketoprofen, naproxen, nimesulide, tolazamide, tolbutamide, tolmentin, zomepirac, aspirin or paracetamol).

(b1) or (b2) is soluble in water and improves the solubility of (a) in the aqueous fluids by increasing the microenvironmental pH of the core above the pKa of (a).

ORGANIC CHEMISTRY - Preferred Components: (b1) Comprises sodium citrate, potassium citrate, tris(hydroxymethyl)aminomethane and/or meglumine. (b2) Comprises sodium citrate, potassium citrate, sodium acetate and/or tris(hydroxymethyl)aminomethane. (c) Comprises mannitol, sorbitol, and/or a carbohydrate comprising sucrose, glucose, fructose, dextrose or lactose. (g) Comprises dibutyl sebacate, diethyl phthalate, dibutyl phthalate, triacetin, triethyl citrate, tributyl citrate, castor oil and/or liquid sorbitol. (d1) Comprises magnesium stearate.

Preferred Method: The mixture obtained by dry blending is passed through standard sieves to obtain uniform particle size to form a core composition. The wet granules are dried at 40-60degreesC for 10 minutes, and are passed through 20-22 standard sieve to break agglomerates and to obtain a core composition having a uniform particle size.

INORGANIC CHEMISTRY - Preferred Components: (b1) Comprises sodium bicarbonate and/or potassium bicarbonate. (b2) Comprises sodium phosphate and/or potassium phosphate. (c) Comprises sodium chloride and/or potassium chloride. (d1) Comprises talc or aerosil.

POLYMERS - Preferred Components: (e) Comprises cellulose acetate, cellulo ethyl cellulose, or polymers of acrylic or methacrylic acid polymer or their esters. (f) Comprises polyvinyl alcohol, polyvinyl pyrrolidone, cellulose ether, polyethylene glycol or polymers of acrylic or methacrylic acid or their esters. (g) Comprises propylene glycol, glycerol and/or polyethylene glycol.

ABEX ADMINISTRATION - Administration is in the form of tablets (claimed). No dosage is given.

EXAMPLE - A pharmaceutical composition for extended release of a weakly acidic drug, glipizide was manufactured using the following ingredients (mg/tablet) as follows. Core tablets comprising (in mg): tris(hydroxymethyl)aminomethane (TRIS) buffer (175), Pearlitol SD 200 (RTM: directly compressible mannitol) (107.6) and sodium chloride (35) was prepared by mixing the ingredients, and then passed through a 30-mesh sieve. Glipizide (10 mg) was mixed with a part of the portion obtained above and after mixing, was passed through a 30-mesh sieve. The blend was

mixed for 10 minutes and Plasdone K29/32 (polyvinyl pyrrolidone) (18 mg) was added to the mixture. The mixture was granulated with ethanol and the resulting wet dough was passed through 18-mesh sieve. The wet granules were dried at 500degreesC for 10 minutes and the dry granules were passed through 22-mesh sieve to break the agglomerates. The granules were then blended with magnesium stearate (5.4 mg), talc (7.2 mg) and aerosil (1.8 mg), and compressed in the form of biconvex tablets having an average weight of 360 mg. - Tablets were placed in a laboratory scale perforated coater along with 200 gm of filter tablets (tablets made using 7 mm round deep concave punches and containing microcrystalline cellulose, starch, dibasic calcium phosphate, magnesium stearate and aerosil) and coated with a coating solution. The coating solution comprising (in g): cellulose acetate (having a molecular weight of 37000 and acetyl value of 40%) (55 g) was prepared by adding it to a mixture of methylene chloride (1534.88 g) and methanol (511.63 g). After the entire polymer was dissolved, Plasdone K29/32 (polyvinyl pyrrolidone) (13.75 g) was added with continuous stirring. Triacetin (5.5 g) and polyethylene glycol (PEG-4400) (11 g) were added and mixed. The coating solution was applied until increase of 12.65 wt.% was obtained. The tablets were dried in an oven for 16 hours at 50degreesC. - The composition was then packed in a 0.04 mm thick aluminum foil laminated with polyvinyl chloride and stored in stability chambers maintained at 40degreesC and 75% relative humidity for 3 months. The release study of the tablets was then conducted in simulated intestinal fluid, pH 6.8 (1000 ml), without enzymes using USP type I apparatus. Comparatively, the tablets were prepared similarly but without the TRIS buffer with a coating till increase of 13.18 wt.% was obtained. It was observed that the comparative tablets did not show any drug release, while the test tablets exhibited extended release of glipizide.

L172 ANSWER 8 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2003-598210 [56] WPIX Full-text
ED 20050531
DNC C2003-162287 [56]
TI Film useful for delivery of pharmaceutical products comprises cereal beta(1-3)beta(1-4) glucan and an active compound
DC B07; D13; D17; D22; P33; P34
IN FIELDER D A; REDMOND M J; FIELDER D; REDMOND M
PA (CEAP-N) CEAPRO INC
CYC 101
PI WO 2003054077 A1 20030703 (200356)* EN 21[0]
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AU 2002347165 A1 20030709 (200428) EN
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EP 1453909 A1 20040908 (200459) EN
US 20050031674 A1 20050210 (200512) EN
JP 2005513140 W 20050512 (200532) JA 30
EP 1790687 A2 20070530 (200735) EN
EP 1453909 B1 20071003 (200765) EN
DE 60222802 E 20071115 (200777) DE
ES 2294180 T3 20080401 (200825) ES
DE 60222802 T2 20080710 (200848) DE

ADT WO 2003054077 A1 WO 2002-CA1896 20021211; US 20050031674 A1 Provisional US 2001-338649P 20011211; AU 2002347165 A1 AU 2002-347165 20021211; DE 60222802 E DE 2002-60222802 20021211; EP 1453909 A1 EP 2002-782583 20021211; EP 1790687 A2 Div Ex EP 2002-782583 20021211; EP 1453909 B1 EP 2002-782583 20021211; DE 60222802 E EP 2002-782583 20021211; ES 2294180 T3 EP 2002-782583 20021211; EP 1453909 A1 WO 2002-CA1896 20021211; US 20050031674 A1 WO 2002-CA1896 20021211; JP 2005513140 W WO 2002-CA1896 20021211; EP 1453909 B1 WO 2002-CA1896 20021211; DE 60222802 E WO 2002-CA1896 20021211; JP 2005513140 W JP 2003-554788 20021211; US 20050031674 A1 US 2004-498568 20040721; EP 1790687 A2 EP 2007-4713 20021211; EP 1453909 B1 Related to EP 2007-4713 20070307; DE 60222802 T2 DE 2002-60222802 20021211; DE 60222802 T2 EP 2002-782583 20021211; DE 60222802 T2 WO 2002-CA1896 20021211

FDT EP 1790687 A2 Div ex EP 1453909 A; DE 60222802 E Based on EP 1453909 A; ES 2294180 T3 Based on EP 1453909 A; EP 1453909 B1 Related to EP 1790687 A; AU 2002347165 A1 Based on WO 2003054077 A; EP 1453909 A1 Based on WO 2003054077 A; JP 2005513140 W Based on WO 2003054077 A; EP 1453909 B1 Based on WO 2003054077 A; DE 60222802 E Based on WO 2003054077 A; DE 60222802 T2 Based on EP 1453909 A; DE 60222802 T2 Based on WO 2003054077 A

PRAI US 2001-338649P 20011211
US 2004-498568 20040721

AB WO 2003054077 A1 UPAB: 20070423

NOVELTY - A film comprises a beta(1-3)beta(1-4) glucan and at least one active agent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) an article coated with at least one layer of the film;

(2) producing the film or an article coated with the film involving mixing an aqueous solution of a beta(1-3)beta(1-4) glucan with at least one active agent, and drying the composition to form the film or applying the composition to an article and drying the applied composition to give the article coated with the film; and

(3) a sweetener composition comprising a beta(1-3)beta(1-4) glucan and a sweetener.

USE - For coating the active agent, in cosmetic, confectionery, medical and pharmaceutical preparations for the delivery of pharmaceutical, medical and confectionery products; and in applying thin films of coating to absorbent surfaces such as tissue for facial and toilet application.

ADVANTAGE - Cereal beta(1-3)beta(1-4) glucan formulates at lower percentages and the thin films are more easily formed with no need for or reduced need for other gums in the finished formulation. beta(1-3)beta(1-4) Glucan sequesters hydrophobic materials and alcoholic extracts, which lends itself to the remarkable oil carrying ratios of cereal beta(1-3)beta(1-4) glucans. The film can coat non-easily wrapped or enrobed objects, or delicate or sensitive materials, especially those that are temperature sensitive.

TECH PHARMACEUTICALS - Preferred Film: The film comprises beta(1-3)beta(1-4) glucan in a concentration of 5-50 (preferably 15-25) wt.%. The film comprises active agent in a concentration of 0.001-50 (preferably 10-25) wt.%.

Preferred Components: The active agent in the film is a pharmaceutically active agent, an anti-microbial agent and/or a flavoring agent. The pharmaceutically active agent is non-steroidal anti-inflammatory drug, an anti-tussive, a decongestant, an anti-histamine, an expectorant, an anti-diarrheal, an H2-antagonist, a nonselective central nervous system depressant or stimulant, an agent that selectively modifies central nervous system function, a drug for treating Parkinson's disease, a narcotic-analgesic, an analgesic-antipyretic and/or a psychopharmacological agent. The anti-microbial agent is triclosan, cetyl pyridinium chloride, sanguinarine, domiphen bromide, quaternary ammonium salt, zinc compound, fluoride, alexidine, octonideine, ethylene diamine tetraacetic acid (EDTA), silver nitrate, thymol, methyl salicylate, eucalyptol and/or menthol. The active agent in the article is a pharmaceutically active agent, an anti-microbial agent and/or a flavoring agent (preferably flavoring agent). The sweetener is effective in producing a favorable stimulatory response in the absence of other sweeteners (preferably Acesulfame K).

Preferred Article: The article is a pharmaceutical formulation, in the form of a tablet or a capsule, a stent, a tissue paper or a dental floss. At least one layer of the article comprises a separate flavoring agent.

ORGANIC CHEMISTRY - Preferred Components: The glucan is derived from cereal grain or a part of cereal grain (preferably cultivars of barley, oat, wheat, rye, sorghum, millet and/or corn). Preferred Method: The glucan and at least one active agent are mixed and they are left undisturbed to form a homogeneous composition (preferably an emulsion), in the absence of an emulsifying agent. The aqueous solution is formed using a 65-100 (preferably 85-100) % pure glucan.

ABEX ADMINISTRATION - The film is administered as a pharmaceutical formulation, in the form of a patch (claimed). The composition is administered orally or topically, in the form of a patch. The composition can also be applied in the form of an aerosol spray to the artide. No dosage given.

EXAMPLE - A pliable beta(1-3)beta(1-4) glucan thin film strips with rapid dissolving action was prepared in two phases A and B. Phase A was prepared by heating purified water (10 g) to 90 degrees C. Methocel (0.4 g) was wet with hot water (10 g) and dispersed well. 1% Liquid beta glucan (100 g) was added immediately. The coloring (FD and C Blue No. 2 (RTM), 0.01 g) was added as per the requirements. Powdered or granular fructose (4 g) was added, followed by the addition of sucralose (1 g). The reaction was mixed well and stirred intermittently for 20 minutes. Phase B was prepared by adding Atmos 300 (RTM) (0.4 g) to 95 % ethanol (1 g), followed by the addition of essential oil flavoring or equivalent (spearmint oil, 0.8 g) and mixing well. Phase A and B were then thoroughly mixed or emulsified and poured to form thin films. The films were allowed to air dry or alternatively were allowed to dry under streams of warm air. The films were dried to a moisture content of 6-8 wt.%, with the resulting water activity (Aw) of 0.150-0.250. The dry films were then cut into strips and removed from the moulds.

L172 ANSWER 9 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2003-148526 [14] WPIX Full-text
ED 20050528
DNC C2003-038400 [14]
TI Fresh filtered cow urine with or without cowdung and bhashma is useful for consumption by ailing patients for health benefit and curing from disease
DC B04
IN JAIN V
PA (JAIN-I) JAIN V; (RAHU-N) RAHUL PROD LTD
CYC 93
PI WO 2002096440 A1 20021205 (200314)* EN 24[0]
<--
AU 2001278671 A1 20021209 (200452) EN
<--
IN 2001MU00516 I3 20050506 (200575) EN
ADT WO 2002096440 A1 WO 2001-IN136 20010727; IN 2001MU00516 I3 IN 2001-MU516 20010601; AU 2001278671 A1 AU 2001-278671 20010727
FDT AU 2001278671 A1 Based on WO 2002096440 A
PRAI IN 2001-MU516 20010601
IN 2001-MU511 20010531
IC ICM A61K035-22

ICS A61K035-78
IPCR A61K0035-22 [I,A]; A61K0035-22 [I,C]
AB WO 2002096440 A1 UPAB: 20060202

NOVELTY - Fresh filtered cow urine from a cow having a hump, a pyramid like structure near its neck with or without cowdung and bhashma is consumed by ailing patients for health benefit and curing from disease.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) Manufacturing herbal medicinal composition (C1) with cow urine in tablet form involves:

(a) mixing the active ingredients in their proportion by weight;

(b) pulversing the active ingredient individually and mixing in the required proportion;

(c) adding excipients, adjuvants, filler in the required proportion on weight basis;

(d) seiveing the above resultant mixture through a mesh 80 to 250;

(e) adding binding agent in the required proportion with the seived mixture;

(f) granulating the moist mass through a granulator to obtain granules;

(g) drying the granules in known manner to obtain dry granules;

(h) adding lubricant and excipient with the dried granules to obtain the correct weight of the granules; and

(i) tableting the granules in a tableting machine.

(2) Manufacturing (C1) in capsule form involves: steps (a) to (c), then mixing the active ingredients with excipients in a grinder for through mixing and grinding. The tested raw material are dried, powdered and sifted and weighed as per batch size. All the ingredients are mixed in a mixer with suitable excipient. The mixed material is sent for capsulation in air-conditioned room with a dehumidifier to have proper atmosphere and a record of weight variation and disintegration is kept;

(3) Manufacturing (C1) in syrup form involves steps (a) and (b). The tested raw materials as per batch size are calculated. Dry powders are sifted. Equivalent amounts of extracts are taken. All the ingredients are mixed in the hot water as per batch size and the syrup is prepared and the active ingredients are mixed properly. Suitable pH is adjusted, flavoring agent, color and stabilizer are added and the volume is made up on the batch size. The whole liquid is filtered through a filter press. The bottles are filled by automatic filling machine, tested for any foreign matter and sealed. Proper records of volume is maintained and bottle used for the batch are properly washed and dried in bottle dryer before use;

(4) Manufacturing (C1) in ointment form involves: steps (a) and (b), then adding ointment base in required proportion on weight basis, and mixing the active ingredients with ointment base and the tested ingredients are weighed as per batch size. The powder material and ointment base and other liquid material are transferred in an ointment mixing machine, which has proper heating arrangement. After proper mixing the ointment is allowed to cool and passed through triple roller machine and the ointment is again transferred in the mixer to have uniform mixing. The ointment is sent for packing after testing;

(5) Manufacturing (C1) in oil form involves: steps (a) and (b). Then tested raw materials are taken and the liquids are mixed in a mixer. The solid raw materials are weighed, powdered and added to the oil bulk. The oil is mixed to have proper product;

(6) Manufacturing (C1) in lepa form involves: steps (a) and (b), and then mixing the active ingredients in a grinder for through mixing. The tested material are taken and the coarse material are powdered dried and sifted, and weighed as per batch size. The liquid materials are filtered. All the powdered weighed material are properly mixed and packed in a bottle as 500 gm and

(7) Manufacturing (C1) in external use eye drops form involves: steps (a), (b) and (d). The Gomayras (cow urine) and til oil are boiled till all the water in Gomayras is completely removed. The contents are well filtered through suitable filtering devise to have shining liquid.

ACTIVITY - Analgesic; Dermatological; Antiinflammatory; Antidiuretic; Anorectic; Cytostatic; Antithyroid; Antidiabetic; Dermatological; Antipsoriatic; Antiasthmatic; Tuberculostatic; Anti-HIV; Tranquilizer; Anticonvulsant; Antimigraine; Antiparkinsonian; Antidiarrheic; Laxative; Antiulcer; Anthelmintic; Hypotensive; Hypertensive; Virucide; Antitussive; Hepatotropic; Antipyretic; Ophthalmological; Antianginal; Immunostimulant, Vasotropic, Gynecological, Cardiant; Antianemic.

MECHANISM OF ACTION - None given.

USE - For curing diseases and for benefit of ailing patients (claimed), in the treatment of skin diseases, obesity, hemolytic jaundice, hepatic Jaundice, obstructive Jaundice, cancer, thyroid, diabetes, eczema, psoriasis, asthma, tuberculosis, urinary calculi, nervous exhaustion, AIDS, blockade of arteries, anxiety, tension, sexual weakness, angina pain, epilepsy, mental retardation, spondolytis, sciatica, blood pressure, female diseases, migraine, paralysis, Parkinsons, indigestion, diarrhea, acidity, giddiness, piles, prostate, constipation, ulcer, gases, anemia, increase of spleen, frequency of urination, mouth diseases, liver disorders, ear-pains and troubles, worms, cold, cough, toothache, scabies, lack of semen, insomnia, nasal disorders, eye troubles, kidney-diseases, headache, menstruation disorder in women, menses irregularities in

women, heart diseases, hepatitis B, tuberculosis, pains, boils, stomach disorder, leprosy, blood disorder, urinary irregularities in men, leucorrhoea, itches, urinary disorders, blood-disorders, blood-deficiency, weakness of liver and spleen, swelling and fever, as a general tonic or brain tonic.

ADVANTAGE - Increases the power of remembrance and intelligence, has several medicinal benefits, showing fast relief from various diseases with no side effects.

TECH PHARMACEUTICALS - Preferred Composition: The excipients are selected from starch, magnesium stearate or di-calcium phosphate. The filler is talc, chinaclay or bentonite. The binding agent is gumtragacanty, sodium methylcellulose or xanathamgum. Preferred method: The urine is collected from healthy cows in clean metal container taking care of any contamination and then filtered eight times through clean cotton cloth with or without herbal ingredients dissolved in it and with or without cow dung/bhashma for direct consumption for ailing patients. The mixing is carried out in a suitable mixer. The pH of the granular mass is adjusted to 6 to 7.5 by using weak alkali.

ABEX ADMINISTRATION - The administration is oral, opthalmogical or topical.

EXAMPLE - A liquid oral composition was prepared comprising (mg) Vikranta Bhasma (1-10), Kancanara Guggul (60-600) and Gojala (cow urine) Concentrate (40-500).

L172 ANSWER 10 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 2003-016924 [01] WPIX Full-text

ED 20050527

DNC C2003-004059 [01]

TI Preparation of oral fast-melt pharmaceutical composition comprises wet granulating cyclooxygenase-2 inhibitory drug with saccharide having high moldability and blending with a saccharide having low moldability

DC A96; B05

IN KARARLI T T; KONTNY M J; LE T T; NYSHADHAM J R; PAGLIERO A J; SASTRY S V; LE TRANG T; NYSHADHAM J R &

PA (KARA-I) KARARLI T T; (KONT-I) KONTNY M J; (LETT-I) LE T T; (NYSH-I) NYSHADHAM J R; (PAGL-I) PAGLIERO A J; (SAST-I) SASTRY S V; (PHAA-C) PHARMACIA CORP; (YAMA-C) YAMANOUCHI PHARMA TECHNOLOGIES INC

CYC 2

PI US 20020119193 A1 20020829 (200301)* EN 17[0]
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TW 256305 B1 20060611 (200726) ZH

ADT US 20020119193 A1 Provisional US 2000-226349P 20000818; US 20020119193 A1 US 2001-932494 20010817; TW 256305 B1 TW 2001-120287 20010817

PRAI US 2001-932494 20010817
US 2000-226349P 20000818
IC ICM A61K031-415
ICS A61K031-341; A61K031-352; A61K031-42; A61K031-44
IPCR A61K0031-435 [I,A]; A61K0031-435 [I,C]; A61K0031-63 [I,C]; A61K0031-635 [I,A]; A61K0047-26 [I,A]; A61K0047-26 [I,C]; A61K0009-00 [I,A]; A61K0009-00 [I,C]
EPC A61K0009-00M18B; A61K0031-435; A61K0031-635; A61K0047-26
NCL NCLM 424/465.000
NCLS 514/277.000; 514/378.000; 514/406.000; 514/473.000
AB US 20020119193 A1 UPAB: 20050527
NOVELTY - Preparation of an oral fast-melt pharmaceutical composition (C) comprises:

(a) wet granulating a selective cyclooxygenase-2 inhibitory drug with a liquid binding agent comprising a saccharide (s1) having high moldability, and

(b) blending a saccharide (s2) having low moldability with the drug.

DETAILED DESCRIPTION - Preparation of an oral fast-melt pharmaceutical composition (C) comprises:

(a) wet granulating a selective cyclooxygenase-2 inhibitory drug with a liquid binding agent comprising a saccharide (s1) having high moldability, and

(b) blending a saccharide (s2) having low moldability with the drug.

Steps (a) and (b) are effected in any order or simultaneously to form granules. The process incorporates agglomeration inhibition of the drug.

An INDEPENDENT CLAIM is included for the composition (C).

ACTIVITY - Analgesic; Antiinflammatory; Antipyretic; Antiarthritic; Antiulcer; Antianemic; Nephrotropic; Hemostatic; Antirheumatic; Antigout; Osteopathic; Dermatological; Immunosuppressive; Antiasthmatic; Antiallergic; Anti-HIV; Virucide; Hepatotropic; Antipsoriatic; Antiseborrheic; Vulnerary; Ophthalmological; Antimigraine; Cytostatic; Antidiabetic; Neuroprotective; Nootropic; Vasotropic; Cerebroprotective; Tranquilizer; Gynecological; Tocolytic.

MECHANISM OF ACTION - Cyclooxygenase-2 inhibitor.

USE - Used for treating inflammation, pain, fever, arthritis, peptic ulcers, gastritis, regional enteritis, ulcerative colitis, diverticulitis, gastrointestinal lesions, gastrointestinal bleeding, coagulation disorders including anemia, hypoprothrombinemia, hemophilia and other bleeding problems, kidney disease, in patients prior to surgery or patients taking anticoagulants, rheumatoid arthritis, spondyloarthropathies, gouty arthritis, osteoarthritis, systemic lupus erythematosus, juvenile arthritis, asthma, bronchitis, menstrual cramps, preterm labor, tendinitis, bursitis, allergic

neuritis, cytomegalovirus infectivity, apoptosis including HIV-induced apoptosis, lumbago, liver diseases such as hepatitis, skin related conditions such as psoriasis, eczema, acne, burns, dermatitis, ultraviolet radiation damage including sunburn, post operative inflammation including that following ophthalmic surgery such as cataract surgery or refractive surgery, inflammatory bowel disease, Crohn's disease, irritable bowel syndrome, migraine headache, periarteritis nodosa, thyroiditis, aplastic anemia, Hodgkin's disease, scleroderma, rheumatic fever, type I diabetes, neuromuscular junction disease including myasthenia gravis, multiple sclerosis, sarcoidosis, nephritic syndrome, nephritic syndrome, Behcet's syndrome, polymyositis, gingivitis, nephritis, hypersensitivity, myocardial ischemia, retinitis, scleritis, episcleritis, conjunctivitis, retinopathies, retinitis, scleritis, episcleritis, uveitis, ocular photophobia, an acute injury to eye tissue, pulmonary inflammation such as associated with viral infections and cystic fibrosis, bone resorption associated with osteoporosis, central nervous system disorders e.g. Alzheimer's disease, neurodegeneration, stroke, ischemia and trauma, vascular dementia, multi-infarct dementia, pre-senile dementia, alcoholic dementia and senile dementia, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome and liver diseases, angiogenesis-related disorders e.g. tumor angiogenesis, neoplasia, metastasis, corneal graft rejection, ocular neovascularization, retinal neovascularization, diabetic retinopathy, macular degeneration, retrolental fibroplasias, glaucoma, gastric ulcer, hemangioma, endometriosis, cancer and fibrosis that occurs with radiation therapy. The composition is also used for treating adenomatous polyps including familial adenomatous polyposis (FAP), dysmenorrhea, premature labor.

ADVANTAGE - The tablet containing (C) disintegrates within 30-300 (especially 30 - 150) seconds in a standard in vitro disintegration assay and within 5-60 (especially 5-25) seconds after placement in the oral cavity. The oral fast-melt tablets containing a cyclooxygenase-2 inhibitory drug of low water solubility, even having high dosage requirements e.g. celecoxib can be prepared efficiently. The dosage form is convenient and easy to swallow. The composition has less harmful side effects than compositions of conventional nonsteroidal anti-inflammatory drugs including gastrointestinal toxicity and gastrointestinal irritation such as upper gastrointestinal ulceration and bleeding, reduced potential for renal side effects such as reduction of renal function leading to fluid retention and exacerbation of hypertension, reduced effect on bleeding times including inhibition of platelet function and a reduced ability to induce asthma attacks in aspirin-sensitive asthmatic patients.

TECH PHARMACEUTICALS - Preferred Composition: The composition

comprises (in wt.%): the selective cyclooxygenase-2 inhibitory drug (1-75, especially 45 - 75), (s1) (1-10, preferably 1-7.5, especially 1-5) and (s2) (10-90, preferably 15-60, especially 25-50), and also comprises a wetting agent (0.05-5, preferably 0.075-2.5, especially 0.25-1), glidant (0.05-5, preferably 0.1-2, especially 0.25-1).

The weight ratio of (s1):(s2) is 2:100-20:100 (preferably 5:100-10:100, especially 5:100-7.5:100).

Preferred Process: Step (b) is effected prior to or simultaneously with step (a). Step (a) comprises fluid bed granulation. The agglomeration inhibition involves pre-wetting the drug prior to step (a) by adding a wetting agent. The process also involves adding a glidant. The process also involves blending the granules with at least one of lubricant, sweetening agent or flavoring agent to form a tableting blend and compressing the blend to form oral fast-melt tablets having a hardness of 1-10 kp.

Preferred Drugs: The selective cyclooxygenase-2 inhibitory drug comprises a compound of formula (I).

R3 = Me or amino;

R4 = H, 1-4C alkyl or alkoxy;

X = N or CR5;

R5 = H or halo, and

Y, Z = C or N atoms defining adjacent atoms of a 5- or 6-membered ring (preferably cyclopentenone, furanone, methylpyrazole, isoxazole or pyridine) optionally substituted by oxo, halo, methyl or halomethyl.

ORGANIC CHEMISTRY - Preferred Components: (s2) Comprises lactose, mannitol, glucose, sucrose or xylitol (preferably mannitol of powder grade). (s1) Comprises maltose, maltitol, sorbitol or oligosaccharides having 2-6 monosaccharide residues. The wetting agent comprises a quaternary ammonium compound, dioctyl sodium sulfosuccinate, polyoxyethylene alkylphenyl ether, poloxamer, polyoxyethylene fatty acid glyceride and oil, polyoxyethylene alkyl ether, polyoxyethylene fatty acid ester, polyoxyethylene sorbitan ester, propylene glycol fatty acid ester, sodium lauryl sulfate, fatty acid or its salt, glyceryl fatty acid ester, sorbitan ester and/or tyloxapol (preferably sodium lauryl sulfate). The glidant comprises silicon dioxide.

ABEX ADMINISTRATION - Administration is orally in the form of a tablet. The dosage of celocoxib is 10-1000 (especially 50-200) mg/day. Administration may be in combination with at least one of opioids (preferably codeine, meperidine, morphine or their derivatives) and other analgesics.

SPECIFIC COMPOUNDS - The selective cyclooxygenase-2 inhibitory drug comprises celecoxib, deracoxib, valdecoxib, rofecoxib, etoricoxib, 2-(3,5-difluorophenyl)-3-(4-(methylsulfonyl)phenyl)-2-

cyclopenten-1-one, (S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid or 2-(3,4-difluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-(4-(methylsulfonyl)phenyl)-3-(2H)-pyridazinone. EXAMPLE - Celecoxib (200 mg), silicon dioxide (2 mg) and low moldability mannitol (165 mg) were de-lumped in a Co-mil producing a drug powder mixture. The drug powder mixture was charged to a Glatt fluid bed processor and preheated. Inlet air was used to provide fluidization of the powder bed, and an aqueous sodium lauryl sulfate solution (4 mg) (2.5 wt.%) and an aqueous maltose solution (20 mg) (15 wt.%) were sprayed onto the fluidized powder bed resulting in wet granules. No material adhered to the walls of the processor. The wet granules were then fluid bed dried. The resulting dried granules were subjected to a milling step through a Co-mil to form a milled granulated. The milled granulate was blended with flavoring agent (Aoesulfame K (2 mg) and peppermint flavor (1 mg)) and lubricants (magnesium stearate (3 mg) and stearic acid (3 mg)) in a tumble blender for about 5 minutes to form a blend. The blend was then compressed using a tooling (11.9 mm), to form tablets having an initial target hardness of 1 kp and a final tablet target weight of 400 mg. - The tablets were subjected to treatment in a chamber through which air at two specified sets of temperatures and relative humidity conditions was circulated. First, air at 25degreesC and a relative humidity of 80 % was circulated through the chamber for 40 minutes and second, air at 50degreesC and a relative humidity of 30 % was circulated through the chamber for 60 minutes. The formulation showed a mean in vitro disintegration time of 1.01 minutes, mean in vivo disintegration time of 23 seconds and final hardness of 3.2-4 kp.

L172 ANSWER 11 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2002-602515 [65] WPIX Full-text
ED 20050526
DNC C2002-170599 [65]
TI Capsule formulation for use as health food or pharmaceuticals, contains liquid containing S-adenosylmethionine or its salt, dispersed or suspended in oil solution, and sealed in gelatin capsule
DC B02; B07
IN FUKAZAWA T; MIYA T; SATO K; SUGII Y; UCHIDA Y; YOKOYAMA A
PA (ARIM-N) ARIMENTO KOGYO KK; (KOJK-C) KOHJIN CO LTD; (MIYA-N) MIYAKO KAGAKU KK
CYC 1
PI JP 2002145783 A 20020522 (200265)* JA 6[0]
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ADT JP 2002145783 A JP 2000-338007 20001106
PRAI JP 2000-338007 20001106

IPCR A61K0031-7042 [I,C]; A61K0031-7076 [I,A]; A61K0047-42 [I,A]; A61K0047-42 [I,C]; A61K0009-48 [I,A]; A61K0009-48 [I,C]; A61P0001-00 [I,C]; A61P0001-16 [I,A]; A61P0019-00 [I,C]; A61P0019-02 [I,A]; A61P0025-00 [I,C]; A61P0025-24 [I,A]

AB JP 2002145783 A UPAB: 20050526

NOVELTY - A capsule formulation contains liquid containing S-adenosylmethionine or its salt, dispersed or suspended in the oil solution. The resulting suspension is sealed in a gelatin capsule.

ACTIVITY - Antidepressant; antiarthritic; hepatotropic. No test details are given for the above mentioned activity.

MECHANISM OF ACTION - None given.

USE - For producing S-adenosylmethionine or its salt, containing capsule formulation which is used as health food or pharmaceutical product. S-adenosylmethionine or its salt, improves depression, arthritis, liver disease (liver cirrhosis).

ADVANTAGE - S-adenosylmethionine or its salt is easily dispersed in edible oil. The capsule formulation is stable as the capsule outer layer hinders the absorption of atmospheric moisture content by S-adenosylmethionine or its salt (which is hydroscopic).

TECH PHARMACEUTICALS - Preferred Ingredients: The oil liquid contains an emulsifier and a thickener in oil. Preferred Amount: The liquid contains 1-50 weight% of S-adenosylmethionine or its salt. The capsule layer contains 0-100 weight parts (wt.pts) of plasticizer in 100 wt.pts of gelatin. Preferred Process: The S-adenosylmethionine or its salt, is dispersed or suspended in the oil solution under vacuum condition. The capsule is produced by dip coating, punching or dropping.

ABEX EXAMPLE - S-adenosylmethionine paratoluene sulfonic acid (I) (35%) was added to an emulsion containing safflower oil (60%), glycerol fatty acid ester (2.5%) and beeswax (2.5%), cooled to 20 degrees C, mixed, stirred, degassed under reduced pressure and a suspension was produced. The content of (I) in the suspension was found to be 100%. Capsule forming solution was obtained by dissolving (in weight parts) gelatin (100), glycerol (35) and caramel pigments (4) in purified water (80) at 65-70 degrees C, and degassing. The capsule forming solution and suspension were used for producing soft gelatin capsule. The molded capsules (600 mg) containing active component (154.6 mg) were dried for 48 hours at 25 +/-2 degrees C, with a supply of dehumidified air and assayed. The result showed that the capsule contained 100.52 mg (100.52%) of (I) in the capsule. After 1,2 and 3 months, the content of (I) was found to be 97.33%, 97.20% and 97.23%, respectively.

L172 ANSWER 12 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 2002-577532 [62] WPIX Full-text

ED 20050526

DNC C2002-163523 [62]
DNN N2002-458008 [62]
TI Manufacture of tabletting die useful in forming, e.g. pharmaceutical pills, involves compacting ferrous powder and sintering the compact
DC B07; M22; P53; P71
IN CARROTT A J
PA (CARR-I) CARROTT A J
CYC 1
PI GB 2370844 A 20020710 (200262)* EN 13[3]
<--
ADT GB 2370844 A GB 2001-24113 20011008
PRAI GB 2000-25113 20001013
IPCR B22F0005-00 [I,A]; B22F0005-00 [I,C]; B30B0015-02 [I,A]; B30B0015-02 [I,C]; C22C0033-02 [I,A]; C22C0033-02 [I,C]
EPC B22F0005-00M; B30B0015-02B; C22C0033-02; C22C0033-02F4
ICO L22F0998:00+B22F5/10; L22F0998:10+B22F3/02+B22F3/10
AB GB 2370844 A UPAB: 20050526

NOVELTY - A tabletting die (1) is manufactured by compacting a ferrous powder to form a compact of near-nett shape, and sintering the compact.

USE - For manufacturing a tabletting die useful in forming pharmaceutical pills , dishwasher tablets, and certain forms of confectionery.

ADVANTAGE - The method reduces material and manufacturing costs and improves material properties to prolong tablet die life. It eliminates the need for current initial manufacturing stages of soft machining and heat treatment. It achieves powder metallurgy products having very high levels of material homogeneity and consistency that provide improved isotropic mechanical characteristics.

DESCRIPTION OF DRAWINGS - The drawing shows a tabletting die formed by the inventive method.

Tabletting die (1)

TECH METALLURGY - Preferred Method: The ferrous powder is mixed with additives prior to compaction. The additives are finely divided lubricants and/or machinability aids. The compaction of the ferrous powder is carried out using a high pressure press. The sintering of the compact is carried out using a high-temperature furnace. The compact is fed slowly through the furnace. The tabletting die is heat treated and tempered following the sintering.
Preferred Materials: The ferrous powder is a steel powder. The ferrous powder comprises (wt.%) carbon (0.8-3), chromium (3-6), vanadium (0.5-3), molybdenum (6-11), cobalt (5-10), tungsten (0.1-3), and silicon (0.3-2).
Preferred Device: The press is hydraulic press.
The furnace is a controlled atmosphere furnace.

L172 ANSWER 13 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2002-291812 [33] WPIX Full-text
ED 20050525
DNC C2002-085652 [33]
TI New compositions for forming films for capsules comprising a poly(alkylene oxide), water and a plasticizer
DC A25; A96; B07; P33
IN HAUNG H; SCHIMITT R; SCHMITT R
PA (UNIC-C) UNION CARBIDE CHEM & PLASTICS TECHNOLOGY
CYC 90
PI WO 2002007711 A1 20020131 (200233)* EN 28[0]
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AU 2001055429 A 20020205 (200236) EN
<--
EP 1305011 A1 20030502 (200331) EN
<--
KR 2003023709 A 20030319 (200346) KO
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BR 2001012599 A 20030701 (200356) PT
<--
JP 2004504445 W 20040212 (200413) JA 45
MX 2003000624 A1 20030901 (200465) ES
<--
ADT WO 2002007711 A1 WO 2001-US12459 20010417; AU 2001055429 A AU 2001-55429 20010417; BR 2001012599 A BR 2001-12599 20010417; EP 1305011 A1 EP 2001-928586 20010417; EP 1305011 A1 WO 2001-US12459 20010417; BR 2001012599 A WO 2001-US12459 20010417; JP 2004504445 W WO 2001-US12459 20010417; MX 2003000624 A1 WO 2001-US12459 20010417; JP 2004504445 W JP 2002-513447 20010417; KR 2003023709 A KR 2003-700858 20030120; MX 2003000624 A1 MX 2003-624 20030121
FDT AU 2001055429 A Based on WO 2002007711 A; EP 1305011 A1 Based on WO 2002007711 A; BR 2001012599 A Based on WO 2002007711 A; JP 2004504445 W Based on WO 2002007711 A; MX 2003000624 A1 Based on WO 2002007711 A
PRAI US 2000-220052P 20000721
IC ICM A61K009-48; C08L071-02
IPCR A61J0003-07 [I,A]; A61J0003-07 [I,C]; A61K0047-34 [I,A]; A61K0047-34 [I,C]; A61K0009-48 [I,A]; A61K0009-48 [I,C]; C08J0005-18 [I,A]; C08J0005-18 [I,C]; C08K0003-00 [I,C]; C08K0003-20 [I,A]; C08K0005-00 [I,A]; C08K0005-00 [I,C]; C08L0071-00 [I,C]; C08L0071-02 [I,A]
EPC A61K0009-48B
AB WO 2002007711 A1 UPAB: 20050525
NOVELTY - New compositions for forming films for capsules comprise a poly(alkylene oxide), water and a plasticizer, are new.

DETAILED DESCRIPTION - A novel composition suitable for forming films useful in the manufacture of capsules comprises:

(a) 49-85 wt.% of a polymer component containing at least 30 wt.%, based on the weight of the polymer component of a poly(alkylene oxide);

(b) 14-50 wt.% by weight of water; and

(c) 1-40 wt.% of a plasticizer component.

INDEPENDENT CLAIMS are also included for:

(1) a thin, easily extensible film suitable for the preparation of capsules comprising:

(a) 49-85 wt.% of a polymer component containing at least 30 wt.%, based on the weight of the polymer component of a poly(alkylene oxide);

(b) 14-50 wt.% water; and

(c) 1-40 wt.% of a plasticizer component, the film having a stress of less than 250 psi at a strain of 100% as determined in accordance with ASTM D882-97 and an Indentation Index of less than 8 as determined by the HH Indentation Test;

(2) a method of forming a film suitable for use in the manufacture of capsules comprising:

(A) forming a blend of:

(i) 49-85 wt.% of a polymer component containing at least 30wt.%, based on the weight of the polymer component of a poly(alkylene oxide),

(ii) 14-50 wt.% water; and

(iii) 0-50 wt.% plasticizer component; and

(B) forming a film having a thickness of 5-50 mls while retaining sufficient water whereby the film has a stress of less than 250 psi at a strain of 100% as determined in accordance with ASTM D882-97 and an Indentation Index of less than 8 as determined by the HH Indentation Test;

(3) a capsule prepared from the film as in (1).

USE - The compositions can be formed into flexible films having properties suitable for replacement of gelatin containing films in the manufacture of soft or hard shell capsules, as a replacement for gelatin based films in the manufacture of capsules, in particular capsules for use in pharmaceutical and other applications where the capsules are to be ingested by humans. The capsules can be used for the oral delivery of pharmaceutically active agents to humans and animals. They can be used in personal care applications, e.g. hair care and skin care formulations, to deliver oils, vitamins, proteins, polymers and other personal care ingredients, to provide bath oil beads, fragrances and time released ingredients, in the manufacture of paint balls and other recreational products, and in a variety of industrial uses, e.g. in the delivery of inks, catalysts, initiators, and enzymes.

ADVANTAGE - The compositions can be formed into films having all of the physical and mechanical properties required to successfully replace gelatin films in the commercial manufacture of capsules. Capsule shells made from the films have a very low water content, typically 0-5% m depending on film composition and resist moisture uptake even in relatively humid conditions while providing excellent mechanical strength. Thus, the films are ideal for encapsulating moisture sensitive materials and meet other standard requirements for capsules including maintenance of capsule shape under external pressure, good solubility in gastro-intestinal fluid and stability for long term storage.

TECH POLYMERS - Preferred Compositions: The poly(alkylene oxide) may be one or more poly(ethylene oxides) having a molecular weight of 100000-8000000 g/gmol. Preferably the polymer component contains at least 50 wt.% poly(ethylene oxide). The compositions can include other polymers, e.g. polysaccharides and derivatives, hyaluronic acid, other cross-linked polyalkylene oxides, polyvinyl pyrrolidones, polycaprolactones, polyvinyl acetates and polycarboxylic acids, polyacrylic acid and polyvinyl acetate.
ORGANIC CHEMISTRY - Preferred Compositions: The water may be present at 14-35 wt.% and the plasticizer at 1-30 wt.%. The plasticizer may be a polyhydric alcohol, a carboxylic acid or a derivative, a sugar or mixtures, e.g. glycerin, propylene glycol, sorbitol, adipic acid, triethyl citrate, glucose, fructose, or xylose.

ABEX EXAMPLE - To a Henschel mixer was added 2500 g of poly(ethylene oxide) having a molecular weight of 300000 (POLYOX WSR N-750 (RTM). Glycerin (830 g) was then slowly added while the mixture was blended until fine granules were obtained. Water (1427 g) was sprayed onto the mixture and the blending was continued for an additional 10 minutes. The mixture was then extruded through a 2-inch wide slot die using a single screw extruder at a screw speed of 10-15 rpm. The temperature of all zones in the extruder and the die were maintained at about 90degreesC. The extruded film was pulled from the slot die through a pair of nip rollers and then was collected on a wind-up roll. The freshly extruded film was placed in an incubator with circulating air under controlled conditions of 50% relative humidity at 25degreesC. Samples were taken at different time intervals to determine the water content in the films. The results showed that the poly(ethylene oxide) based films lose water readily . Ellipsoidal shaped capsules were prepared from these films on a small mold that simulates the action of an encapsulation rotary die. The film was heated gently just prior to sealing when water content was below 20% and required no heating when water content was about 30%. The resulting capsules had strong seals. The finished (dry) capsules appeared opaque and had a smooth surface and a strong seam. They retained their shapes well under

external force. The capsules were filled with vegetable oil or poly(ethylene glycol). These capsules ruptured within 30 minutes in a dissolution test as in U.S. Pharmacopeia, 24 rev, U.S. Pharmacopeia Convention: Rockville, MD, 2000, 1941-1942, by stirring (50 rpm) at 37degreesC in 0.1N HCl (1000 ml). In general the capsules dissolved faster with higher plasticizer contents and thinner shells.

L172 ANSWER 14 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2002-239386 [29] WPIX Full-text
ED 20050525
CR 2001-316159; 2001-316166; 2001-316167; 2001-328328; 2002-280174
DNC C2002-072187 [29]
TI Coating for a composition (preferably a solid or non-aqueous liquid composition) comprises a foam component having a matrix comprising a polymeric material that is stable upon contact with air and unstable in water
DC B07
IN CORRAND D M; SOMMERVILLE-ROBERTS N; YORK D W
PA (PROC-C) PROCTER & GAMBLE CO
CYC 93
PI WO 2001024779 A1 20010412 (200229)* EN 35[0]
<--
AU 2000078536 A 20010510 (200143) EN
<--
GB 2355008 A 20010411 (200242) EN
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BR 2000014532 A 20020604 (200246) PT
<--
EP 1237542 A1 20020911 (200267) EN
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CN 1378444 A 20021106 (200316) ZH
<--
JP 2003510454 W 20030318 (200321) JA 38
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MX 2002003446 A1 20020901 (200370) ES
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ADT WO 2001024779 A1 WO 2000-US27338 20001004; GB 2355008 A GB 1999-23393 19991005; AU 2000078536 A AU 2000-78536 20001004; BR 2000014532 A BR 2000-14532 20001004; CN 1378444 A CN 2000-813942 20001004; EP 1237542 A1 EP 2000-968654 20001004; BR 2000014532 A WO 2000-US27338 20001004; EP 1237542 A1 WO 2000-US27338 20001004; JP 2003510454 W WO 2000-US27338 20001004; MX 2002003446 A1 WO 2000-US27338 20001004; JP 2003510454 W JP 2001-527778 20001004; MX 2002003446 A1 MX 2002-3446 20020404

FDT AU 2000078536 A Based on WO 2001024779 A; BR 2000014532 A Based on WO 2001024779 A; EP 1237542 A1 Based on WO 2001024779 A; JP 2003510454 W Based on WO 2001024779 A; MX 2002003446 A1 Based on WO 2001024779 A

PRAI GB 1999-23393 19991005

IC ICM C11D017-04
ICS A61K007-50

IPCR A61K0008-00 [I,A]; A61K0008-00 [I,C]; A61K0008-04 [I,A]; A61K0008-04 [I,C]; A61K0008-30 [I,C]; A61K0008-34 [I,A]; A61K0008-66 [I,A]; A61K0008-72 [I,C]; A61K0008-73 [I,A]; A61K0008-86 [I,A]; A61Q0019-10 [I,A]; A61Q0019-10 [I,C]; C08J0009-00 [I,C]; C08J0009-30 [I,A]; C11D0011-00 [I,A]; C11D0011-00 [I,C]; C11D0017-00 [I,A]; C11D0017-00 [I,C]; C11D0017-04 [I,A]; C11D0017-04 [I,C]; C11D0017-06 [I,A]; C11D0017-06 [I,C]; C11D0003-22 [I,A]; C11D0003-22 [I,C]; C11D0003-37 [I,A]; C11D0003-37 [I,C]

EPC A61K0008-02C; A61K0008-04F; A61Q0019-10; C08J0009-30; C11D0003-22E; C11D0003-37; C11D0003-37C8H; C11D0011-00B6; C11D0017-00D

AB WO 2001024779 A1 UPAB: 20050525

NOVELTY - Coating for a composition (preferably a solid or non-aqueous liquid composition) comprises a foam component having a matrix comprising a polymeric material that is stable upon contact with air and unstable in water.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(1) a composition (preferably solid or non-aqueous liquid) enclosed by the coating;

(2) an absorbent article comprising the coating;

(3) a pre-dosed amount of a solid composition (partially) enclosed by a coating or a non-aqueous liquid composition enclosed by a coating in the form of a pouch or hollow 3-dimensional coating;

(4) preparation of the coating comprising obtaining the polymeric material, chemically or physically introducing gas into the polymeric material and optionally addition of an additional ingredient and/or solvent (preferably water) and removing the solvent; and

(5) preparation of a flexible coating, where the matrix is (partially) formed from polymeric material and contains cells, comprising:

(a) obtaining a mixture of polymeric material and a liquid (preferably water);

(b) evaporation of the liquid to form spacings that form the inner area of the matrix cells by heating or submitting the mixture to pressure and increased temperature, subsequently reducing pressure causing the liquid to evaporate.

USE - The coating is useful for (partially) enclosing a solid or non-aqueous composition to protect the composition during storage and/or handling against e.g. impact, moisture, air, light, temperature change or segregation of ingredients, for delivering

active ingredients to an aqueous environment e.g. detergent active ingredients, granules, tablets or flowable product , and to control the rate and moment of release, dissolving or dispersion of a solid or non-aqueous solution (claimed). The coatings can also be incorporated into absorbing articles to release active ingredients to the skin when in contact with water, or bodily fluids, e.g. diapers, wipes, catamenial, plasters, and bandages.

TECH PHARMACEUTICALS - Preferred Coating: The coating partially or completely disintegrates, disperses and/or denatures in water. The coating has an elastic modulus of less than 10, preferably less than 1 GN/m2.

Preferred Foam: Foam component has a relative density of 0.05-0.9, preferably 0.1-0.8. Foam comprises a mixture of polymeric mixture and additional ingredient (preferably cleaning product, fabric care, personal care, pharmaceutical or cosmetic ingredient, especially a dye, enzyme, perfume, surfactant, brightener, bleach, bleach activator, fabric softener, fabric conditioner, antibacterial agent and/or effervescing system). Foam component may also comprise a stabilizer, acidic material and/or plasticizer (preferably glycerol, ethylene glycol, diethylene glycol, propylene glycol or sorbitol).

Preferred Composition: Composition is a cleaning, fabric care, personal care, pharmaceutical or cosmetic composition.

Pre-dosed composition is in the form of a tablet , granule, or flowable composition

POLYMERS - Preferred Polymer: Polymeric material comprises a water soluble and/or water dispersible polymer (preferably polyvinyl alcohol, polysaccharide, polycarboxylic acid, cellulose, modified cellulose and/or gums).

ABEX EXAMPLE - Polyvinyl alcohol (PVA; 50 g), glycerol (30 g) and citric acid (20 g) were mixed. Water (50 ml) was added gradually over 2 minutes to obtain a smooth gel. Mixing speed increased and water (10-20 ml) was added until a PVA foam formed. The PVA foam was spread into moulds avoiding collapse of the structure. The filled moulds were placed in a thermally insulated box 1/3 full of dry ice, and left to freeze for 5 hours. Samples were placed in a vacuum freeze drier for 24 hours, then the dried sample was removed from the moulds.

L172 ANSWER 15 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2002-237038 [29] WPIX Full-text
ED 20050525
CR 1992-433328; 1998-051418; 1998-296700; 1998-321446
DNC C2002-071690 [29]
TI Manufacture of pharmaceutical cellulose capsules comprises gelatinizing aqueous solution of thermogelling cellulose ether composition in pins, and drying gelatinized solution with air moving

over pins in opposite direction
DC A11; A96; B07
IN ANDERSON J B; ANDREW C S; GROSSWALD R R
PA (SCHB-C) SCHERER TECHNOLOGIES INC R P
CYC 2
PI US 6337045 B1 20020108 (200229)* EN 28[18]
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IN 2003CH00056 I4 20070727 (200780)# EN
ADT US 6337045 B1 CIP of US 1991-708023 19910531; US 6337045 B1 Cont of US 1992-893091 19920529; US 6337045 B1 Cont of US 1995-377669 19950124; US 6337045 B1 US 1997-896873 19970421; IN 2003CH00056 I4 Div Ex IN 1997-CH559 19970317; IN 2003CH00056 I4 IN 2003-CH56 20030117
FDT US 6337045 B1 Cont of US 5698155 A
PRAI US 1997-896873 19970421
US 1991-708023 19910531
US 1992-893091 19920529
US 1995-377669 19950124
IN 2003-CH56 20030117
IC ICM A61J003-00
IPCR A61J0003-07 [I,A]; A61J0003-07 [I,C]; B29C0033-00 [N,C]; B29C0033-06 [I,A]; B29C0033-06 [I,C]; B29C0033-30 [I,A]; B29C0033-30 [I,C]; B29C0033-36 [N,A]; B29C0033-44 [N,A]; B29C0033-44 [N,C]; B29C0033-56 [N,C]; B29C0033-60 [N,A]; B29C0035-02 [I,A]; B29C0035-02 [I,C]; B29C0035-04 [I,A]; B29C0035-04 [I,C]; B29C0035-08 [N,A]; B29C0035-08 [N,C]; B29C0041-14 [I,A]; B29C0041-14 [I,C]
EPC A61J0003-07B3; B29C0033-06; B29C0033-30; B29C0035-02M; B29C0035-04; B29C0041-14
ICO L29C0033:36; L29C0033:44; L29C0033:60; L29C0035:04C; L29C0035:08B; L29C0201:00
NCL NCLM 264/402.000
NCLS 264/297.800; 264/305.000; 264/310.000; 264/327.000; 264/405.000; 264/DIG.037; 425/174.600; 425/272.000; 425/804.000
AB US 6337045 B1 UPAB: 20050902
NOVELTY - Pharmaceutical cellulose capsules are manufactured by gelatinizing an aqueous solution of a thermogelling cellulose ether composition in capsule body pins and capsule cap pins to form capsule bodies and capsule caps. Then, the gelatinized solution is dried by moving the pins through a kiln with air moving over the pins in a direction opposite that of the movement of the pins.

DETAILED DESCRIPTION - Manufacture of pharmaceutical cellulose capsules uses an aqueous solution of a thermogelling cellulose ether composition, and capsule body pins and capsule cap pins as molds. Each pin is dipped in the solution to a dip line to gelatinize the solution on the pin and form a capsule part of thermally gelatinized solution. The gelatinized solution is then dried by moving the pins

through a kiln with air moving over the pins. The air moves in a direction opposite the direction of movement of the pins. Thus, the gelatinized solution on the pins encounters humid air during an early stage of drying, and drier air during a later stage of drying. The capsule bodies and capsule caps are then removed from the pins.

USE - For manufacturing pharmaceutical cellulose capsules.

ADVANTAGE - The inventive method provides capsules with improved uniformity and rigidity. It avoids capsules imperfections, e.g. wrinkles, starred ends and corrugations, which result in capsule either breaking, failing to separate, or jamming in the high-speed filling machines.

DESCRIPTION OF DRAWINGS - The figure shows a schematic of the inventive method.

TECH POLYMERS - Preferred Method: The gelatinized solution on each pin is dried by heating a pin via a bar or by a radiant heat in an early stage of drying. Thus, the heat at an inner surface of a capsule part and the humid air surrounding the capsule part causes the capsule to dry slowly from the inside out.
The air is moved over the capsule body pins at one rate and over the capsule cap pins at a different rate. The pins within the kiln are heated to achieve a predetermined air temperature profile within the kiln. The flow of air within the kiln is controlled to achieve a predetermined humidity profile within the kiln.
Preferred Conditions: The air enters the kiln at 125-180degreesF with a humidity of 0.006-0.012 lb water/lb air. The drier air is approximately149degreesF while the humid air is 111degreesF.

L172 ANSWER 16 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2002-097617 [13] WPIX Full-text
ED 20050524
DNC C2002-030409 [13]
TI Single pass, continuous, automated system used for production of pharmaceutical granulation includes powder and liquid feeders, twin screw wet granulator and chopper device and conveyor
DC B02; B07; P33; P41; P64; Q76
IN FESSEHAIE M; GHEBRE-SEL-LASSIE I; GHEBRE-SELLASSIE I; LODAYA M; MOLLAN M J; PATHAK N; SHAH U
PA (FESS-I) FESSEHAIE M; (GHEB-I) GHEBRE-SELLASSIE I; (LODA-I) LODAYA M; (MOLL-I) MOLLAN M J; (PATH-I) PATHAK N; (WARN-C) WARNER LAMBERT CO; (WARN-C) WARNER LAMBERT CO LLC
CYC 95
PI WO 2001089679 A2 20011129 (200213)* EN 41[6]
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AU 2001061588 A 20011203 (200221) EN
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     US 6499984      B1 20021231 (200305)  EN
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     NO 2002005592   A  20030122 (200320)  NO
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     BR 2001011001   A  20030408 (200329)  PT
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     US 20030090039  A1 20030515 (200335)  EN
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     KR 2003011340   A  20030207 (200339)  KO
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     CZ 2002003764   A3 20030618 (200347)  CS
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     SK 2002001625   A3 20030911 (200363)  SK
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     EP 1351760      A2 20031015 (200368)  EN
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     ZA 2002009283   A  20031126 (200402)  EN  44
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     HU 2003002312   A2 20031128 (200405)  HU
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     JP 2004501679   W  20040122 (200411)  JA  68
     CN 1458862      A  20031126 (200413)  ZH
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     MX 2002011556   A1 20030401 (200415)  ES
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     NZ 522722       A  20040625 (200445)  EN
     IN 2002MN01626  P3 20041211 (200530)  EN
ADT  WO 2001089679 A2 WO 2001-US15597 20010514; US 6499984 B1
     US 2000-576373 20000522; US 20030090039 A1 Div Ex US
     2000-576373 20000522; IN 2002MN01626 P3 WO 2001-US15597 ; AU
     2001061588 A AU 2001-61588 20010514; BR 2001011001 A
     BR 2001-11001 20010514; CN 1458862 A CN 2001-811310
     20010514; EP 1351760 A2 EP 2001-935498 20010514; JP
     2004501679 W JP 2001-585912 20010514; NZ 522722 A NZ
     2001-522722 20010514; NO 2002005592 A WO 2001-US15597
     20010514; BR 2001011001 A WO 2001-US15597 20010514;
     CZ 2002003764 A3 WO 2001-US15597 20010514; SK 2002001625
     A3 WO 2001-US15597 20010514; EP 1351760 A2 WO
     2001-US15597 20010514; HU 2003002312 A2 WO 2001-US15597
     20010514; JP 2004501679 W WO 2001-US15597 20010514;
     MX 2002011556 A1 WO 2001-US15597 20010514; NZ 522722 A
     WO 2001-US15597 20010514; CZ 2002003764 A3 CZ 2002-3764
     20010514; SK 2002001625 A3 SK 2002-1625 20010514; US
     20030090039 A1 US 2002-290964 20021108; ZA 2002009283 A
     ZA 2002-9283 20021114; IN 2002MN01626 P3 IN 2002-MN1626
     20021115; KR 2003011340 A KR 2002-715721 20021121; NO
     2002005592 A NO 2002-5592 20021121; MX 2002011556 A1
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MX 2002-11556 20021122; HU 2003002312 A2 HU 2003-2312 20010514

FDT US 20030090039 A1 Div ex US 6499984 B; AU 2001061588 A Based on WO 2001089679 A; BR 2001011001 A Based on WO 2001089679 A; CZ 2002003764 A3 Based on WO 2001089679 A; SK 2002001625 A3 Based on WO 2001089679 A; EP 1351760 A2 Based on WO 2001089679 A; HU 2003002312 A2 Based on WO 2001089679 A; JP 2004501679 W Based on WO 2001089679 A; MX 2002011556 A1 Based on WO 2001089679 A; NZ 522722 A Based on WO 2001089679 A

PRAI US 2000-576373 20000522
US 2002-290964 20021108

AB WO 2001089679 A2 UPAB: 20060118

NOVELTY - Single pass continuous processing system comprises powder and liquid feeders (2, 4), a twin-screw wet granulator-chopper device (1), a means for conveying the wet granulation, loading it onto a dryer belt and levelling the granulation, a drying apparatus, a means of conveying the dried granulation, a mill and a control means.

DETAILED DESCRIPTION - Single-pass, continuous processing system (I) comprises:

(a) powder and liquid feeders to provide at least one pharmaceutically active ingredient and additives and at least one liquid;

(b) a twin-screw wet granulator-chopper device in a housing having a non-extruding opening at the outlet end, for granulation of the ingredients received from the feeders into a wet granulation form;

(c) a means for conveying the wet granulation from the outlet of the twin screw granulator, loading it on to a dryer belt and levelling the granulation to the desired height;

(d) a drying apparatus for receiving the wet granulation from the dryer belt and drying it using dielectric energy;

(e) a means of conveying the dried granulation from the drying tunnel for size reduction;

(f) a mill for reducing the dried granulation to particles of the desired size; and

(g) a control means for controlling the process variables of at least one of the powder and liquid feeder, the twin-screw wet granulator- chopper, the conveying, loading and levelling device, the drying apparatus, the conveying means, and the mill to optimize the production of the pharmaceutical granulation.

INDEPENDENT CLAIMS are included for the following:

(1) a drying apparatus comprising a conveying belt for receiving and transporting the granulation to be dried, a drying tunnel containing a source of dielectric energy and electrodes for producing an alternating electric field to heat the granulation, a source of heated and cooled air, a flow control mechanism for controlling the flow of heated and cooled air in the tunnel and a

control means for controlling the energy and air flow in the tunnel, and

(2) a twin-screw wet granulator-chopper comprising a housing containing feed points for solids and liquids, twin screws having inter-engaging threads adapted to rotate in the same or opposite directions within the housing, a motor for rotating the twin screws, an open end for discharging the granulation and a means for chopping the granulation into discrete particles, and

(3) production of a high dose pharmaceutical granulation which comprises feeding a powder containing the pharmaceutically active agent to the twin-screw wet granulator-chopper with a liquid for granulation, conveying the powder and liquid to the first mixing element via the first conveying element and mixing to form a wet mass, and conveying the wet mass to the chopper element via the second conveying element to convert it into a granulation.

USE - (I) is useful for the continuous manufacture of a pharmaceutical granulation of a wide variety of active agents, especially of nelfinavir mesylate.

ADVANTAGE - The system allows for continuous preparation of pharmaceutical granulations on a manufacturing scale at high dosage rates.

DESCRIPTION OF DRAWINGS - The figure shows a schematic diagram of the apparatus

Twin-screw wet granulator-chopper (1)
Powder feeder (2)
Pump (3)
Liquid feeder (4)
Liquid reservoir (5)
Housing (9)
Discharge bin (17)

TECH CHEMICAL ENGINEERING - Preferred Apparatus: The dielectric energy is radio frequency or low or high frequency microwave energy. The flow of air in the tunnel is co- or counter-current with the direction of travel of the granulation on the travel belt. The drying apparatus has a gradient with progressively decreasing moisture content in the granulation. The screw has reverse and or thread-free zones including kneading discs, or combing, gear, pin or calender gap mixers. The chopping means is flush with or extends beyond the open end of the granulator-chopper. The pitches of the conveying elements are reduced progressively along the length of the conveying element(s). The powder feed is a side-stuffer and the liquid feed a liquid injector.

The twin-screw wet granulator-chopper preferably comprises a first conveying element of a given pitch, a second conveying element, placed after the first conveying element and having at least one pitch which is less than those of the first conveying element, a

first mixing element positioned between the first and second conveying elements, at least one chopping element positioned after the second conveying element and a housing surrounding the elements which has an inlet and a non-extruding opening at the outlet. Optionally there is a third conveying element, with at least one pitch being less than those of the second conveying element, placed before the chopping element and after a second mixing element. The powder and first liquid feeder are both coupled to the twin screw wet granulator chopper at a position aligned with the first conveying element and a second liquid feeder is aligned at a position between the first conveying element and the first mixing element. The first mixing element is positioned immediately adjacent to both the first and second conveying elements. On-line monitoring is performed to control the moisture content of the granulation, the liquid feeder being controlled to adjust the moisture content. Uniformity of distribution of the active ingredient is monitored on-line at various locations throughout the system.

Preferred Method: The wet mass is mixed by a second mixer positioned between the second conveyor and a third conveyor before the chopping process. The temperature of the twin- screw wet granulator chopper is maintained at 15-90degreesC. The the granulation may be milled before drying to reduce the particle size.

Preferred Product: (I) is used to prepare a granulation of nelfinavir mesylate in combination with calcium silicate in a ratio of 4:1 and water for granulation.

ABEX EXAMPLE - A pre-blend of an investigational drug and excipients was prepared by mixing the weighed ingredients in a 16 qt V-blender. The blend was fed into the twin-screw wet granulator-chopper from a loss-in-weight solid feeder via a side-suffer mechanism adjusted to give a feed rate of 11.4 kg/hour. An aqueous solution containing a surfactant was injected into the granulator-chopper using a piston pump at a rate of 8.64 l/hour (a total of 6.8 l was used). The temperature of the granulator-chopper was maintained at 26degreesC and the screw speed was 177 rpm at a maximum torque of 19%. - The granulation was produced at an output rate of 18.2 kg/hour and dried in a tray drier at 50degreesC for 9 hours to reduce the moisture content from 13.6% to 1.0%.

The dried granulation was milled in a hammer mill and the final blend of product was prepared by mixing the milled granulate with excipients in a V-blender before tabletting in a conventional press. Physical testing showed that the tablets formed from the granulation exhibited good compressibility and disintegration and good dissolution, giving complete release of the drug within 20 minutes.

AN 1997-042953 [04] WPIX Full-text
ED 20050514
DNC C1997-013650 [04]
TI Mfg hard shell pharmaceutical capsules from aq thermo-gelling cellulose ether compsn - by dipping moulding pin into compsn and allowing to gelatinise and dry; adhesion of dried compsn to mould broken before sepd from it to minimise damage to moulded compsn
DC A32; A96; B07
IN GROSSWALD R R; THORNOCK S D
PA (GSTE-N) GS TECHNOLOGIES INC
CYC 18
PI WO 9639292 A1 19961212 (199704)* EN 55[7]
<--
EP 773858 A1 19970521 (199725) EN [1]
<--
ADT WO 9639292 A1 WO 1996-US8428 19960603; EP 773858 A1 EP 1996-917938 19960603; EP 773858 A1 WO 1996-US8428 19960603
FDT EP 773858 A1 Based on WO 9639292 A
PRAI US 1995-461835 19950605
IPCR A61J0003-07 [I,A]; A61J0003-07 [I,C]; B29C0033-44 [I,A]; B29C0033-44 [I,C]; B29C0041-14 [I,A]; B29C0041-14 [I,C]; B29C0041-34 [I,C]; B29C0041-42 [I,A]
EPC A61J0003-07B3; B29C0033-44B2; B29C0041-14; B29C0041-42
AB WO 1996039292 A1 UPAB: 20050514

Pharmaceutical cellulose capsules are mfd from an aq thermo-gelling cellulose ether compsn using capsule body pins and capsule cap pins as moulds. Each pin has an axis and a dome. A pin (22) is dipped in the soln to a dip line and allowed to gelatinise and dry on the pin so it defines a part capsule (28) with a wall with a dome end. The adhesion between the part capsule and the pin is broken, they are sepd and the part capsule trimmed to make an open ended part capsule. The pins are transported through a closed transport path during the above sequence. In one aspect the part capsule is sepd by applying a pushing force to it.

Appts for performing as above has the pins mounted on a transport system for moving through a dipping section, a drying section, an automatics section and a trimmer. The automatics section has a gripper/stripper with two rotatable arms for sepg the part capsule from the pin.

In two modifications the gripper/stripper is replaced with a separate gripper (24) and stripper or a separate break adhesion section and a stripper.

USE - Mfg hard shell pharmaceutical cellulose capsules

ADVANTAGE - Part capsules are sepd from pins without damage.

ABDT WO9639292

Pharmaceutical cellulose capsules are mfd from an aq thermo-gelling cellulose ether compsn using capsule body pins and capsule cap pins as moulds. Each pin has an axis and a dome. A pin (22) is dipped in the soln to a dip line and allowed to gelatinise and dry on the pin so it defines a part capsule (28) with a wall with a dome end. The adhesion between the part capsule and the pin is broken, they are sepd and the part capsule trimmed to make an open ended part capsule. The pins are transported through a closed transport path during the above sequence. In one aspect the part capsule is sepd by applying a pushing force to it.

Appts for performing the process has the pins mounted on a transport system for moving through a dipping section, a drying section, an automatics section and a trimmer. The automatics section has a gripper/stripper with two rotatable arms for sepg the part capsule from the pin.

The gripper/stripper is replaced with a separate gripper (24) and stripper or a separate break adhesion section and a stripper.

USE

Hard shell pharmaceutical cellulose capsules are obtd.

ADVANTAGE

Part capsules are sepd from pins without damage.

PREFERRED METHOD

The pushing force is mechanical, applied air pressure or applied vacuum. The capsule part is trimmed so as to sacrifice a section between the dip line and a trim line.

PREFERRED APPARATUS

The gripper has either two opposed bars each carrying spring loaded gripper blocks or opposed spiked faces. The gripper/stripper translates towards/away from a pin along the pin axis. It has two grooved gripper arms and a grooved stripper arm.

L172 ANSWER 18 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1987-007155 [01] WPIX Full-text
ED 20050424
CR 1985-171315
DNC C1987-002881 [21]
DNN N1987-005340 [21]
TI Treating material with hot air in closed drum - with periodic removal of air under vacuum, esp. for effervescent granules contg. solid food acid
DC B07; J08; Q76
IN GERGELY G; GERGELY I; GERGELY T
PA (GERG-I) GERGELY G
CYC 16
PI WO 8607547 A 19861231 (198701)* DE 36[2]
<--
DD 247376 A 19870708 (198747) DE

<--
EP 258258 A 19880309 (198810) DE 14
<--
JP 63501137 W 19880428 (198823) JA
<--
EP 258258 B 19890329 (198913) DE
<--
DE 3662584 G 19890503 (198919) DE
<--
US 4876802 A 19891031 (199002) EN 13
<--
US 4911930 A 19900327 (199018) EN
<--
JP 08000186 B2 19960110 (199606) JA 10
<--

ADT WO 8607547 A WO 1986-EP359 19860619; EP 258258 A EP 1986-904132 19860619; JP 63501137 W JP 1986-503694 19860619; JP 08000186 B2 JP 1986-503694 19860619; JP 08000186 B2 WO 1986-EP359 19860619; US 4876802 A US 1986-877112 19860623; US 4911930 A US 1989-297405 19890117

FDT JP 08000186 B2 Based on JP 63501137 A; JP 08000186 B2 Based on WO 8607547 A

PRAI CH 1985-4267 19851003
AT 1983-4465 19831221
CH 1985-2640 19850621

AB WO 1986007547 A UPAB: 20050424
Material (A) is treated in a closed drum by intermittently, (a) passing through or over the heap of (A) a flow of hot gas and (b) removing the gas by means of a vacuum pump, until the required degree of treatment has been reached. The new feature is that the gas stream is compressed before entering the drum and/or is loaded with a gaseous treatment agent. The jacket of the drum is pref. heated. Also new is an appts. for this process.

USE/ADVANTAGE - The method is esp. used to make effervescent granulate formulations contg. a toxicologically acceptable acid, but some examples refer to prepn. of pharmaceutical compsns. This method allows relatively rapid and very uniform treatment (and opt. drying) of bulk (A), even where this is a normally-sensitive material.

ABEQ (0007)
US 4876802 A UPAB 20050424
Agitated powders or granules are heat treated in a closed drum by driving a hot mixt. of carrier gas and vapourised treatment agent (TA) through the agitated particles. The particles are below the b.pt. of the TA. The TA condensed on the

particles is evacuated and drawn out of the drum under vacuum or a reduced press corresponding to the b.ot. of the TA.
A vacuum of 600-900 mbar is pref. prevailing in the drum during at least part of the treatment. The gas flow impinges on the particles in a finely distributed manner. The particles are agitated every 60-300 secs.

USE - For the partial dehydration of particles contg. water of hydration using an alcohol as TA; to bind water and finely divided reactant to toxicologically acceptable water soluble coarse grained acid used in the prodn. of tablets.

ABEQ (0008)
US 4911930 A UPAB 20050424
Effervescent granulate comprises coarse particles of 1 or more toxicoligcal water-soluble acid to which 1 or more unreacted alkali metal or alkaline earth metal carbonate or bicarbonate and 1 or more water-soluble F-cotng. cpd. is bound through a binding layer. Binding layer comrpises the reaction prod. of the acid and (bi)carbonate. Opt. salt is embedded in the binding layer. F-contg. cpd. comprises disodium monofluorophosphate.

ADVANTAGE - Uniform drying of a powder charge is obtd. even when sensitive substances are used. @(13pp)@

L172 ANSWER 19 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1980-48213C [28] WPIX Full-text
ED 20050418
TI Moulding one piece hard gelatin capsules for pharmaceutical liq. - spreading gelatin layer inside closed mould of increasing vol.
DC B07; P33; P34
IN VOEGLE G
PA (BOSC-C) BOSCH GMBH ROBERT
CYC 6
PI BE 881883 A 19800616 (198028)* FR
<--
DE 2909230 A 19800918 (198039) DE
<--
GB 2043581 A 19801008 (198041) EN
<--
FR 2450604 A 19801107 (198051) FR
<--
US 4263251 A 19810421 (198119) EN
<--
IT 1129733 B 19860611 (198745) IT
<--
PRAI DE 1979-2909230 19790309

IPCR A61J0003-07 [I,A]; A61J0003-07 [I,C]; A61K0009-48 [I,A]; A61K0009-48 [I,C]
EPC A61J0003-07
NCL NCLM 264/503.000
NCLS 264/523.000; 264/524.000; 264/571.000
AB BE 881883 A UPAB: 20050418
Fluid gelatin is spread in a layer which lines the interior surface of a hollow mould. Pref. an appropriate measure of fluid gelatin is spread as a layer inside a closed mould, the resulting one-piece capsule is dried and then ejected from the mould.
The fluid gelatin is pref. spread as a layer by a combination of blowing with compressed air and progressively enlarging the vol. of the mould cavity to draw out the gelatin. The injection of hot air into the newl-formed capsule can be alternated with connecting the interior of the gel capsule to vacuum. This promoters rapid drying of the gelatin.
It is an inexpensive process for making hard gelatine capsules in one piece. This eliminates the need to seam tog. two-piece capsules and the problems associated with such seams.
FS CPI; GMPI
MC CPI: B04-B04A; B12-M11
CMC UPB 20050418
M1 *01* M423 M720 N100 R031 R032 R033 R034 R036 R038 R043 V751 V752 V753 V754 M902
M6 *02* R031 R112 R531 M902

L172 ANSWER 20 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1979-H6535B [36] WPIX Full-text
ED 20050419
TI Pharmaceutical tablets dust extractor - has vertically curved channel with top nozzle forming thin flat jet
DC P33
IN BITYUKOV V K; KOLODESHNO V N
PA (VOTE-C) VORON TECHN INST
CYC 1
PI SU 634745 A 19781215 (197936)* RU
<--
ADT SU 634745 A SU 1977-2507149 19770715
IC IC A61J005-00
AB SU 634745 A UPAB: 20050419
Improved reliability of dust removal from each tablet formed by a press is due to the pneumatic chamber in the form of channel (1) curved in the vertical plane. The top of the channel features a jet forming nozzle (2) and discharge branch (3) connected to the channel by profiled rod guides (4). The chamber is set at an angle to the plane of press table, and compressed air is fed to the nozzle (2)

forming a thin flat jet. The air flow induces a partial vacuum near the nozzle for drawing dust from tablets (8).
FS GMPI

L172 ANSWER 21 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1975-H1663W [28] WPIX Full-text
ED 20050416
TI Revolving tablet press - has working region completely surrounded by cabin with air filter and dust aspiration
DC P71
PA (KORC-C) KORSCH SPEZIALFAB EMIL
CYC 1
PI DE 2363921 A 19750703 (197528)* DE
<--
ADT DE 2363921 A DE 1973-2363921 19731219
PRAI DE 1973-2363921 19731219
IC IC B30B011-08
EPC B30B0011-08; B30B0015-00M
AB DE 2363921 A UPAB: 20051230
Revolving tablet press has the drive fitted in the pedestal on which is built a cabin dust-tightly surrounding the whole working region of the press. The material container is outside the cabin, in which are dust filters for air fed into the cabin and suction nozzles for the dust-laden air, especially at dust deposition points. The cabin has a tablet outlet opening with an air barrier where air is likewise sucked out. Preferably a material feed connection with shutoff valve is on the roof of the cabin, which can be connected to a press.-equalization duct to a closed material container which can be screwed to the material feed connection. The pharmaceutical press operates completely dust-free and ensures higher purity of the tablets produced .
FS GMPI

L172 ANSWER 22 OF 22 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1966-06907F [00] WPIX Full-text
ED 20050412
TI Soft elastic capsules with substantially air-free
DC B00
PA (UPJO-C) UPJOHN CO
CYC 1
PI US 3081234 A (196800)* EN
ADT US 3081234 A US 1961-125251 19610719
EPC A61J0003-07; A61K0009-48C
NCL NCLM 424/453.000
NCLS 053/289.000; 053/452.000; 053/467.000; 053/486.000
AB US 3081234 A UPAB: 20050412

Filled soft elastic capsules prep. by charging a dosage filling of dry medicament in granular or pilule form into preformed soft capsule body, closing capsule sufficiently to permit escape of air but not capsule fill from vol. to be enclosed, applying localised press. to inwardly deform surface of capsule, completing closure while maintaining inward deform. and then removing deform.
Method applied to Colton die plate capsule machine wherein gelatine sheet is placed over lower die plate having perforated cavities and wherein lower capsule members formed by deforming gelatine sheet into cavities by application of vacuum below cavities. After the dry medicament filling has been placed in the lower capsule member and immediately prior to placing upper sealing gelatine sheet thereover, vacuum is interrupted and compressed air applied to perforations to expel trapped air. After air has been expelled and upper and lower capsule portions united, the vacuum is restored. Supply and duration of pressure controlled by time delay relay actuated by the press. itself and operating a 3-way valve. Elimination of trapped air renders capsules more acceptable.

=> D L173 1-41 MAX

L173 ANSWER 1 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2007-600097 [57] WPIX Full-text
ED 20070907
CR 2005-365846
DNC C2007-215368 [57]
TI Annular unsupported catalyst useful for preparing acrolein by heterogeneously catalyzed partial gas phase oxidation comprises active composition having metal oxide
DC A41; E17; J04
IN MULLER-ENGEL K J; PETZOLDT J
PA (BADI-C) BASF AG
CYC 1
PI US 20070142223 A1 20070621 (200757)* EN 15[1]
ADT US 20070142223 A1 Provisional US 2003-520660P 20031118; US 20070142223 A1 Div Ex US 2004-974831 20041028; US 20070142223 A1 US 2007-627573 20070126
FDT US 20070142223 A1 Div ex US 7208636 B
PRAI DE 2003-10353954 20031118
IPCI B01J0021-00 [I,A]; B01J0021-00 [I,C]
EPC B01J0023-888M; B01J0035-00B; B01J0035-02P; C07C0045-35+47/22
NCL NCLM 502/248.000

AB US 20070142223 A1 UPAB: 20070907

NOVELTY - An annular unsupported catalyst comprises active composition having a metal oxide.

DETAILED DESCRIPTION - An annular unsupported catalyst comprises active composition having a metal oxide of formula Mo12WaCobFecBidSieKfOn (I).

a = 1-3;

b = 3-8;

c = 1-4;

d = 0.5-1.5;

e = 0-10;

f = 0-0.2; and

n = a number which is determined by the valency and frequency of the elements in the composition of formula (I) other than oxygen.

In the multimetal oxide composition of formula (I) the following molar ratios are: Co/Fe is 2-3.5, and Co/Mo is 0.4-0.7.

USE - For preparing acrolein by heterogeneously catalyzed partial gas phase oxidation.

ADVANTAGE - The catalyst at high propene hourly space velocity on the fixed catalyst bed achieves the given propene conversion at reduced hotspot temperature of the fixed catalyst bed, and increased target product selectivity.

TECH INORGANIC CHEMISTRY - Preferred Components: The annular unsupported catalyst comprises an annular geometry where a length is 2-11 (preferably 2.8-3.2) mm, an external diameter is 2-11 (preferably 5.5-7) mm and a wall thickness is 0.5-5 (preferably 3.5-5) mm. The annular unsupported catalyst is in the form of rings whose external diameter is 2-10 mm, whose internal ring diameter is at least 1 mm, whose wall thickness is of 0.5-2 mm and whose length is 2-10 mm. The annular unsupported catalyst has a specific surface area of 5-20 (preferably 5-15) m2/g and a total pore volume of 0.1-1 (preferably 0.1-0.8) cm3/g.

ABEX DEFINITIONS - Preferred Definitions: - a = 1.5-2.5 (preferably 2-2.5); - b = 5-8 (preferably 6-8); - c = 2-4 (preferably 2.5-3.5). - The molar ratio of Co/Fe is 2-3.3 (preferably 2-3), and the molar ratio of Co/Mo is 0.45-0.7.

EXAMPLE - Tungstic acid (72.94 wt.% of W, 209.3 kg) was stirred in portions into an aqueous bismuth nitrate solution (775 kg) in nitric acid (11.2 wt.% of Bi; free nitric acid from 3-5 wt.%; mass density: 1.22-1.27 g/ml) at 25degreesC. The resulting aqueous mixture was subsequently stirred at 25degreesC for a further 2 hours and subsequently spray-dried. The spray-drying was effected in a rotating disk spray tower in countercurrent at a gas inlet temperature of 300 plus minus 10degreesC and a gas outlet temperature of 100 plus minus 10degreesC. The resulting spray powder (particle size a substantially uniform 30 microns) which had an ignition loss of 12 wt.% (ignite at 600degreesC under air for 3

hours) was subsequently converted to a paste in a kneader using 16.8 wt.% of water and extruded to extrudates of diameter 6 mm. These were cut into sections of 6 cm, dried under air on a 3-zone belt dryer at a residence time of 120 minutes at 90-95degreesC (zone 1), 115degreesC (zone 2) and 125degreesC (zone 3), and then thermally treated at 780-810degreesC (calcined; in a rotary tube oven flowed through by air (0.3 mbar of reduced pressure, capacity 1.54 m3, 200 m3 (STP) of air/h)). The desired phases were WO3 (monoclinic) and Bi2W2O9; the presence of gamma-Bi2WO6 (Russellite) was undesired. Thus, the compound gamma-Bi2WO6 was detectable by a reflection in the X-ray powder diffractogram after the calcination, the preparation had to be repeated and the calcination temperature increased within the temperature range specified or the residence time increased at constant calcination temperature, until the disappearance of the reflection was achieved. - The preformed calcined mixed oxide obtained in this way was ground so that the X50 value of the resulting particle size was 5 mm. The ground material was then mixed with Sipemat type (RTM: finely divided SiO2) (1 wt.%) to obtain a composition (c1). A solution (s1) was prepared by dissolving ammonium heptamolybdate tetrahydrate (81.5 wt.% of MoO3, 213 kg) at 60degreesC with stirring in water (600 l) and the resulting solution was mixed while maintaining the 60degreesC and stirring with an aqueous potassium hydroxide solution (46.8 wt.% of KOH, 0.97 kg) at 20degreesC. A solution (s2) was prepared by introducing an aqueous iron(III) nitrate solution (14.2 wt.% of Fe, 116.25 kg) at 60degreesC into an aqueous cobalt(II) nitrate solution (12.4 wt.% of Co, 334.6 kg). Subsequently, while maintaining the 60degreesC, solution (s2) was continuously pumped into the initially charged solution (s1) over a period of 30 minutes. Subsequently, the mixture was stirred at 60degreesC for 15 minutes. A Ludox silica gel (19.16 kg) (46.80 wt.% of SiO2, density: 1.36-1.42 g/ml, pH 8.5-9.5, maximum alkali content 0.5 wt.%) were then added to the resulting aqueous mixture, and the mixture was stirred afterward at 60degreesC for a further 15 minutes. Subsequently, the mixture was spray-dried in countercurrent in a rotating disk spray tower (gas inlet temperature: 400 plus minus 10degreesC, gas outlet temperature: 140 plus minus 5degreesC) to obtain a composition (c2), which had an ignition loss of 30 wt.% (ignite under air at 600degreesC for 3 hours) and a substantially uniform particle size of 30 pm. - The composition (c1) was mixed homogeneously with the composition (c2) in the amounts required for a multimetal oxide active composition of Mo12W2Co7Fe3Bi1Si1.6K0.08Oy. In the obtained composition, an additional 1 wt.% of TIMREX P44 type (RTM: finely divided graphite) was mixed homogeneously. The resulting mixture was then conveyed in a compactor to obtain compactate which had a hardness of 10 N and a substantially uniform particle size of 400 pm - 1 mm. The compactate

was subsequently mixed with, a further 2 wt.% of the same graphite and subsequently compressed in a Kilian rotary tableting press under a nitrogen atmosphere to give an annular shaped unsupported catalyst precursor body of geometry having a side crushing strength of 16.3 N. For the final thermal treatment, the shaped unsupported catalyst precursor bodies (1000 g) were heated in a muffle furnace flowed through by air (capacity 60 l, 1 l/h of air per gram of shaped unsupported catalyst precursor body) initially from room temperature (25degreesC) to 190degreesC at a heating rate of 180degreesC/h. This temperature was maintained for 1 hour and then increased to 210degreesC at a heating rate of 60degreesC/h. The temperature of 210degreesC was in turn maintained over 1 hour before it was increased to 230degreesC at a heating rate of 60degreesC/h. This temperature was likewise maintained for 1 hour before it was increased to 265degreesC, again at a heating rate of 60degreesC/h. The temperature of 265degreesC was subsequently likewise maintained over 1 hour. Afterward, the furnace was initially cooled to room temperature and the decomposition phase thus substantially completed. The furnace was then heated to 465degreesC at a heating rate of 180degreesC/h and this calcination temperature maintained over 4 hours to obtain annular shaped unsupported catalyst. - The obtained catalyst was tested for a heterogeneously catalyzed partial oxidation of propene to acrolein. The results showed that all the advantages were on the side of the obtained catalyst fixed catalyst bed. The selectivity of acrylic acid by-production was 8.5 mol.% (based on propene converted).

L173 ANSWER 2 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2006-017030 [02] WPIX Full-text
ED 20060125
CR 2003-165808
DNC C2006-005120 [02]
TI Composition exhibiting reduced malodor, useful to treat e.g. osteoarthritis, comprises: chondroitin derived from marine life; citric acid; and silicon dioxide
DC A11; A96; B04
IN EBUBE N K; MARK W A
PA (AMHP-C) WYETH
CYC 1
PI US 20050256080 A1 20051117 (200602)* EN 3[0]
ADT US 20050256080 A1 Provisional US 2001-274806P 20010309; US 20050256080 A1 Div Ex US 2002-94096 20020308; US 20050256080 A1 US 2005-120887 20050503
FDT US 20050256080 A1 Div ex US 6906045 B
PRAI US 2005-120887 20050503
US 2001-274806P 20010309

US 2002-94096 20020308
IPCR A61L0009-01 [I,C]; A61L0009-013 [I,A]; A61L0009-014 [I,A]
EPC A61L0009-013; A61L0009-014; C08B0037-00P2D
NCL NCLM 514/054.000
AB US 20050256080 A1 UPAB: 20060125
NOVELTY - Composition (I) exhibiting reduced malodor comprises chondroitin derived from marine life; citric acid; and silicon dioxide.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a solid dosage form comprising (I); and

(2) a composition which does not exhibit malodor comprising chondroitin sulfate derived from marine life.

ACTIVITY - Antiarthritic; Osteopathic.

No biological data given.

MECHANISM OF ACTION - None given.

USE - The chondroitin derived from marine life is useful as chondroprotective agents for the treatment of osteoarthritis and related diseases, tissue repair and cartilage regeneration.

ADVANTAGE - (I) lacks malodor associated with chondroitin and has improved consumer acceptability and enhanced patient compliance.

TECH ORGANIC CHEMISTRY - Preferred Components: The chondroitin is chondroitin sulfate derived from shark cartilage. The citric acid is 0.5-10 (preferably 1.5) wt.%, the silicon dioxide is 0.01-2 (preferably 0.2) wt.% and the flavorant is up to about 10 (preferably 3.3) wt.%, all based upon 100 wt.% of (I). (I) further comprises a flavorant (natural and/or artificial flavorants) and glucosamine or its salt, where the weight ratio of glucosamine or its salt to chondroitin is 5:4.

ABEX EXAMPLE - Glucosamine sulfate and chondrotin sulfate mixture (5:4) was prepared by mixing glucosamine hydrochloride (750 g) and chondroitin sulfate (600 g). The mixture was placed into the feed hopper of a Fitzpatric IR-520 chilsonator. The chilsonator converted the mixture into a compacted solid. The chilsonator was operated at a roll speed of 6 rpm, roll pressure of 1250 psig, vertical screw speed of 150 rpm, and horizontal screw speed of 15 rpm. The compacted product formed in the chilsonator was passed through a Fitzpatric M5A mill and the granulated product collected. The mill was operated at a rotor speed of 300 rpm with a 4 bar rotor and a 0.050 inch rasping screen. The relative humidity was 57% and the temperature was 75degreesF. The chondroitin sulfate/glucosamine hydrochloride mixture, sodium starch glycolate (30 mg) and magnesium stearate (15 mg) were added to the silicon dioxide/lemon extract/citric acid blend and blended for 3 minutes. The resulting powder blend was compressed into a tablet at a suitable compression pressure using a rotary tablet press and standard tooling. The resulting

tablet did not exhibit any malodor, differing substantially from that exhibiting by the initial chondroitin sulfate component.

L173 ANSWER 3 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2005-221891 [23] WPIX Full-text
ED 20050708
DNC C2005-070949 [23]
TI Delivery dosage form for oral osmotic delivery of therapeutic compounds having limited solubility in aqueous environment , e.g. glipizide, comprises active agent having solubility limitation, and meglumine as solubilizing agent
DC A96; B05
IN BHATT P P; BRYAN J W; KIDANE A; RAY S K; BHATT P; BRYAN J; RAY S
PA (BHAT-I) BHATT P P; (BRYA-I) BRYAN J W; (KIDA-I) KIDANE A; (RAYS-I) RAY S K; (SHIR-N) SHIRE LAB INC
CYC 107
PI US 20050053653 A1 20050310 (200523)* EN 22[10]
WO 2005023228 A1 20050317 (200523) EN
EP 1660051 A1 20060531 (200636) EN
JP 2007504270 W 20070301 (200718) JA 28
ADT US 20050053653 A1 US 2003-655725 20030905; EP 1660051 A1 EP 2004-783203 20040907; WO 2005023228 A1 WO 2004-US28875 20040907; EP 1660051 A1 WO 2004-US28875 20040907; JP 2007504270 W WO 2004-US28875 20040907; JP 2007504270 W JP 2006-526205 20040907
FDT EP 1660051 A1 Based on WO 2005023228 A; JP 2007504270 W Based on WO 2005023228 A
PRAI US 2003-655725 20030905
IPCI A61K0031-64 [I,A]; A61K0031-64 [I,C]; A61K0047-14 [I,A]; A61K0047-14 [I,C]; A61K0047-16 [I,C]; A61K0047-18 [I,A]; A61K0047-20 [I,A]; A61K0047-20 [I,C]; A61K0047-34 [I,A]; A61K0047-34 [I,C]; A61K0047-38 [I,A]; A61K0047-38 [I,C]; A61K0009-20 [I,A]; A61K0009-20 [I,C]; A61K0009-30 [I,C]; A61K0009-36 [I,A]; A61P0003-00 [I,C]; A61P0003-10 [I,A]
IPCR A61K0009-00 [I,A]; A61K0009-00 [I,C]; A61K0009-24 [I,A]; A61K0009-24 [I,C]; A61K0009-48 [I,A]; A61K0009-48 [I,C]
EPC A61K0009-00L4
NCL NCLM 424/463.000
AB US 20050053653 A1 UPAB: 20060122
NOVELTY - An oral osmotic pharmaceutical delivery dosage form comprises active agent(s) having solubility limitations, and meglumine as a solubilizing agent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(a) preparation of solid oral dosage form by mixing active agent(s) with meglumine and binder solution, spraying to form granules, drying the granules in a fluid bed, dry screening the granules, lubricating the granules by adding lubricating agent, dry

blending to effect adequate distribution of the tablet lubrication agent, and compressing on a rotary tablet press to obtain a solid oral dosage form;

(b) delivery of pharmaceutical dosage unit to a mammal, e.g. human, by orally administering the above osmotic pharmaceutical delivery dosage form; and

(c) treatment of abnormal condition in a mammal by orally administering the above osmotic pharmaceutical delivery dosage form to the mammal, and monitoring the effectiveness of the treatment.

USE - For oral osmotic delivery of therapeutic compounds having limited solubility in aqueous environment, e.g. glipizide or other hydrophobic drugs.

ADVANTAGE - The inventive dosage form enables safe and effective oral osmotic delivery of e.g. glipizide.

TECH PHARMACEUTICALS - Preferred Components: The active agent is albendazole, albuterol, acyclovir, adriamycin, carbamazepine, oxcarbazepine, amiodarone, amlodipine, amphetamine, amphotericin B, atorvastatin, atovaquone, azithromycin, baclofen, bicalutamide, busulfan, butenafine, calcipotriene, calcitriol, camptothecin, capsaicin, carotene, celecoxib, cerivastatin, chlorpheniramine, cimetidine, ciprofloxacin, cisapride, cetirizine, clarithromycin, clemastine, codeine, cyclosporin, danazol, dantrolene, dexchlorpheniramine, digoxin, dirithromycin, donepezil, efavirenz, ergotamine, etodolac, etoposide, famotidine, fentanyl, finasteride, fluconazole, flurbiprofen, fluvastatin, fosphenyloin, frovatriptan, gabapentin, gemfibrozil, glibenclamide, glyburide, glimepiride, griseofulvin, halofantrine, ibuprofen, irinotecan, isotretinoin, itraconazole, ivermectin, ketoconazole, ketorolac, lamotrigine, angiotensin converting enzyme (ACE) or NEP inhibitor, fenofibrate, fexofenadine, flutamide, glipizide, glyburide, isradipine, loratadine, lovastatin, melphalan, nifedipine, leflunomide, loperamide, lycopene, mifepristone, mefloquine, methadone, methoxsalen, metronidazole, miconazole, midazolam, miglitol, mitoxantrone, nabumetone, nalbuphine, naratriptan, nelfinavir, nilutamide, nizatidine, oxaprozin, paclitaxel, pentazocine, pioglitazone, pizotefin, pravastatin, probucol, pyridostigmine, raloxifene, rofecoxib, repaglinide, rifapentine, rimexolone, rizatriptan, rosiglitazone, saquinavir, sibutramine, sildenafil citrate, simvastatin, sirolimus, spironolactone, sumatriptan, tacrine, tacrolimus, tamoxifen, tamsulosin, targretin, tazarotene, teniposide, terbinafine, tiagabine, tizanidine, topiramate, topotecan, toremifene, tramadol, tretinoin, troglitazone, trovafloxacin, verteporfin, vigabatrin, vitamin A, vitamin D, vitamin E, vitamin K, zafirlukast, zileuton, zolmitriptan, zolpidem, zopiclone, proton pump inhibitor (such as lansoprazole, esomeprazole, omeprazole, and rabeprazole), MAP kinase inhibitor, ICE inhibitor such as pralnacasan, pseudoephedrine, indomethacin,

naproxen, estrogen, testosterone steroid, phenyloin, ergotamine, cannabinoid, or salt, isomer, prodrug, or derivative of these active agents. The active agent may be diltiazem HCl, verapamil HCl, metoprolol succinate, quetiapine fumarate, valganciclovir HCl, theophylline, or naproxene sodium. The active agent is preferably glipizide.

Preferred Composition: The oral dosage form may comprise high hydrophilic-lipophilic balance (HLB) surfactant as co-solubilizer. In other embodiment, the dosage form has a semipermeable wall that maintains its integrity during pharmaceutical delivery and has passageway(s) connecting the core with the external environment, and a core surrounded by the wall and comprising active agent(s), non-swelling solubilizing agent(s), and non-swelling osmotic agent(s). The dosage form may comprise a plasticizer.

POLYMERS - Preferred Components: The semipermeable wall is made of water-insoluble polymer, e.g. cellulose acrylate, cellulose ethyl ether, cellulose diacrylate, cellulose triacrylate, cellulose diacetate, cellulose triacetate, mono-, di- and tricellulose alkyl, mono-, di- and tricellulose aryl, or preferably cellulose acetate. The semipermeable wall also contains 0.01-20 wt.% plasticizer, e.g. dibenzyl phthalate, dihexyl phthalate, butyl octyl phthalate, 6-11C straight-chain phthalate, di-isononyl phthalate, di-isodecyl phthalate, triacetin, dioctyl azelate, epoxidized tallate, tri-isoctyl trimellitate, tri-isononyl trimellitate, sucrose acetate isobutyrate, or epoxidized soybean oil. The semi-permeable wall represents a weight gain to the dosage form of 2-15%.

ORGANIC CHEMISTRY - Preferred Components: The non-swelling solubilizing agent comprises meglumine. The non-swelling solubilizing agent comprises high HLB surfactant. The surfactant is sodium lauryl sulfate (SLS). The plasticizer, e.g. propylene glycol (PG), a mixture of 25-75% triethyl citrate (TEC) and 75-25% PG, Tween 80 or other polyoxyethylene sorbitan ester, triacetin, diethyl phthalate, polyethylene glycol, mineral oil, tributyl sebacate, glycerol, or preferably TEC.

Preferred Process: The process may include coating the solid oral dosage form with a semi-permeable wall, forming a passageway in the semi-permeable wall either manually or by addition of a water-soluble substance to the composition of semi-permeable wall.

ABEX EXAMPLE - A dosage form containing glipizide (2.27 wt.%), Xylitol CM90 (45 wt.%), Maltrin M150 (wet, 1.33 wt.%), Maltrin M150 (dry, 39.4 wt.%), meglumine (5 wt.%), SLS (5 wt.%), magnesium stearate (1 wt.%), and stearic acid (1 wt.%) was prepared.

L173 ANSWER 4 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2005-038460 [04] WPIX Full-text
ED 20050707

DNC C2005-012692 [04]
TI Composition useful for the administration an extended release pharmaceutical composition for the treatment of bacterial infection comprises active agent, polymer and acid in specific amounts
DC A18; A25; A96; B05
IN CHOW S; CHOW S L; LIN J L; LIN J L Y; WONG D
PA (BIOK-N) BIOKEY INC
CYC 106
PI US 20040247679 A1 20041209 (200504)* EN 10[1]
WO 2004108162 A2 20041216 (200504) EN
US 7063862 B2 20060620 (200641) EN
CN 1812768 A 20060802 (200682) ZH
ADT US 20040247679 A1 US 2003-454240 20030603; WO 2004108162 A2 WO 2004-US15953 20040521; CN 1812768 A CN 2004-80015472 20040521
PRAI US 2003-454240 20030603
IPCI A61K0031-70 [I,A]; A61K0031-70 [I,C]; A61K0031-7042 [I,C]; A61K0031-7048 [I,A]; A61K0009-16 [I,A]; A61K0009-20 [I,A]; A61K0009-20 [I,C]; A61K0009-20 [I,A]
IPCR A61K0031-429 [I,C]; A61K0031-43 [I,A]; A61K0031-545 [I,A]; A61K0031-545 [I,C]; A61K0031-60 [I,A]; A61K0031-60 [I,C]; A61K0031-65 [I,A]; A61K0031-65 [I,C]; A61K0031-7028 [I,C]; A61K0031-704 [I,A]; A61K0031-7042 [I,C]; A61K0031-7048 [I,A]; A61K0009-20 [I,A]; A61K0009-20 [I,C]
EPC A61K0009-20H4; A61K0009-20H4B; A61K0009-20H6F2; A61K0031-43; A61K0031-545; A61K0031-60; A61K0031-65; A61K0031-704; A61K0031-7048
NCL NCLM 424/465.000
NCLS 424/468.000; 424/480.000; 514/028.000; 514/029.000; 514/152.000; 514/165.000; 514/192.000; 514/200.000; 514/355.000; 514/651.000
AB US 20040247679 A1 UPAB: 20060121

NOVELTY - A pharmaceutical composition (C1) (comprises (wt.%): active agent; polymer (0.1-4.9); and acid (0.1-30). The composition has a zero order release profile of the active agent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) an extended release pharmaceutical composition (C2) comprises: a core of a pharmaceutical mixture; and a coating layer of a coating material. The pharmaceutical mixture comprises, the active agent (preferably antibiotic (10-95 wt.%)), polymer (0.1-4.9); and acid (0.1-30); and

(2) preparation of the composition involving: forming a core having a pharmaceutical mixture comprising (C1); and coating the core with a coating layer of a coating material.

ACTIVITY - Antibacterial; Auditory; Respiratory-Gen.

MECHANISM OF ACTION - Bacterial growth inhibitor.

USE - For the administration an extended release pharmaceutical composition for the treatment of bacterial infection

(claimed); in treating common infections of the middle ear and upper respiratory tract.

ADVANTAGE - The composition has a zero order release profile of the active agent. The composition provides extended release of the active ingredient. The composition provides delayed or sustained release forms of drug active ingredients, low concentration of soluble polymers often result in high drug dissolution, better drug release, good absorption, and acid stability at variable pH environments throughout the whole gastrointestinal (GI) tract.

TECH PHARMACEUTICALS - Preferred Components: The active agent (10-95 wt.%), is antibiotic, erythromycin, clarithromycin, azithromycin, amoxicillin, tetracycline, anti-hypertensive, calcium channel blocker, beta-blocker, analgesic, anti-neoplastic agent, anti-malarial, non-steroidal anti-inflammatory drugs (NSAID), diuretic and/or anti-arrythmia agent and their derivatives.

Preferred Composition: (C1) comprises (wt.%): erythromycin derivative (30-80), hydroxypropyl methylcellulose (1.5-4.5) and carboxylic acid (0.1-10); and clarithromycin (30-80), hydroxypropyl methylcellulose (1.5-4.5), citric acid (0.1-10), and lactose (10-50). The pharmaceutical mixture comprises (wt.%): clarithromycin (30-80), hydroxypropyl methylcellulose (1.5-4.5), citric acid (0.1-30), and lactose (10-50).

Preferred Method: The method further involves: compressing the composition into a dosage form selected from oral dosage form and/or solid dosage form. The core is formed by mixing pharmaceutical mixture and compressing the mixture into a tablet; by a technique selected from dry granulation and wet granulation.

POLYMERS - Preferred Components: In (C1), the polymer is component A (preferably hydroxypropyl methylcellulose of high viscosity grade with viscosity at least 5000 cps, especially polyvinyl pyrrolidone of high viscosity grade with viscosity at least about 55 cps, particularly a mixture of hydroxypropyl methylcellulose and polyvinyl pyrrolidone). The component A is hydrophilic polymer, polyvinyl pyrrolidone, hydroxypropyl cellulose, hydroxypropyl methylcellulose (0.1-4.5), alkyl cellulose, ethyl cellulose, methyl cellulose, cellulose ether, vinyl acetate/crotonic acid copolymer, methacrylic acid copolymer, maleic anhydride/methyl vinyl ether copolymer, hydroxymethyl methacrylate, polyethylene oxide, maltodextrin, natural gum and/or xanthan gum and their derivatives. The coating material is enteric polymer, plasticizer, rapid-disintegrating coating material, methacrylate copolymer, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate, hydroxypropyl methylcellulose succinate, carboxymethylethylcellulose, cellulose acetophthalate, disintegrant, polyethylene glycol and/or propylene glycol, and their derivatives (preferably Eudragit (RTM; methacrylic acid copolymer)). In the pharmaceutical mixture, the polymer is component A.

ORGANIC CHEMISTRY - Preferred Composition: (C1) and the pharmaceutical mixture further comprises at least one excipient. Preferred Components: The acid is organic acid, carboxylic acid, keto acid, alpha-hydroxy acid and/or beta-hydroxy acid, and their derivatives. The excipient is filler, extender, binder, blending agent, surfactant, emulsifier, dispersing agent, defoamer, lubricant, nonstick agent, blender, coating material, glidant, anti-sticking agent, diluent, dye, pigment, dispersant and/or wetting agent and their derivatives. The coating material is dye, pigment and/or colorant and their derivatives. The coating material is provided for rapid disintegration of the active agent at pH at least 5.

ABEX ADMINISTRATION - The pharmaceutical mixture is administered in the form of granules, spherical beads, tablets, pellets, particles, coated beads, coated pellets and/or coated particles (claimed). The composition is administered in a oral dosage form. The antibiotic is administered in a dosage of 500 mg/day.

EXAMPLE - Clarithromycin (500 mg) extended release tablet was prepared by wet granulation. The tablet was prepared by passing a mixture of polyvinyl pyrrolidone (0.1-0.9 wt.%), half of the anhydrous lactose (30-45 wt.%) needed, and citric acid (0.5-4.5 wt.%) through a 25 mesh screen and the mixture was added into a granulator. Micronized clarithromycin (500 mg) and the other half of the anhydrous lactose (30-45 wt.%) were added into the granulator to be mixed for about 10 minutes. The resulting blend/mixture was mixed with purified water, the granulating liquid, inside the granulator and mixed until granules were formed. The granules were dried at 50 degrees C overnight. The dried granules were equipped with mesh screen. The screened granules were mixed with talc (0.5-5 wt.%), colloidal silicon dioxide (0.1-5 wt.%), hydroxypropyl methylcellulose (3-4 wt.%) and magnesium stearate (0.1-5 wt.%) for approximately 12 minutes totally and then compressed into tablets using a rotary press fitted with oval shaped punches. The compressed tablet was coated with Eudragit L30 D-55 (RTM) and propylene glycol by first mixing Eudragit L30 D-55 and propylene glycol in purified water and then applying the resulting solution to the compressed tablet using a pan coater. The compressed tablet was coated with the coating material until a theoretical coating level of approximately 1% was obtained. The resulting tablet together with reference formulation were tested in phosphate buffer (pH 5). The release profile for the tablet was found to be 100% after 12 hours. The results demonstrated a zero order release of clarithromycin.

L173 ANSWER 5 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2004-765414 [75] WPIX Full-text

ED 20050707
CR 2003-300150
DNC C2004-268255 [75]
TI Cleaning station for compression unit detached from rotary table press comprises separate cleaning fluid devices connected to compression unit including dies, feeding device and tablet discharge device
DC A96; B07
IN BOECKX J; CHRISTIAENS D; VAN ZEGBROECK A; VOGELEER J
PA (COUR-N) COURTOY NV
CYC 1
PI US 20040207107 A1 20041021 (200475)* EN 17[9]
ADT US 20040207107 A1 Div Ex US 2001-960739 20010924; US 20040207107 A1 US 2004-754510 20040112
FDT US 20040207107 A1 Div ex US 6676863 B
PRAI WO 2001-IB1631 20010905
IPCR B29B0011-00 [I,C]; B29B0011-12 [I,A]
NCL NCLM 264/039.000
NCLS 264/109.000; 425/225.000; 425/227.000; 425/229.000
AB US 20040207107 A1 UPAB: 20050707

NOVELTY - A cleaning station comprising at least two separate cleaning fluid devices each having a connection piece for detachable connection with a corresponding connection piece provided on a compression unit and communicating with an enclosure of the compression unit, is new.

DETAILED DESCRIPTION - A cleaning station for cleaning a compression unit (14) detached from a rotary tablet press comprises at least two separate cleaning fluid devices each having a connection piece for detachable connection with a corresponding connection piece provided on the compression unit and communicating with an enclosure of the compression unit. The cleaning fluid devices are arranged for the supply of cleaning fluid to the compression unit and for the drainage of cleaning fluid from the compression unit. The compression unit comprises dies arranged circumferentially in a rotary die table and each associated with at least a first punch having a first end receivable in the die through an opening of the die; a feeding device for the supply of material to be compressed into the dies; and a tablet discharge device for removal of compressed material in the form of tablets.

An INDEPENDENT CLAIM is also included for cleaning a compression unit detached from a rotary tablet press by connecting separate cleaning fluid device(s) with a compression unit to communicate with an enclosure of the compression unit; and subsequently supplying cleaning fluid to the enclosure of the compression unit from the cleaning fluid device(s).

USE - The cleaning station is used for cleaning a compression unit detached from a rotary table press (claimed).

ADVANTAGE - The invention provides a tablet press by which the time required for cleaning of the press between batches is reduced and by which the risk of contamination of the surrounding environment as well as exposure of the operator to the product may be reduced to a minimum.

DESCRIPTION OF DRAWINGS - The figure shows a perspective view of a rotary tablet press of the invention with the housing cover partly removed.

Press housing (2)
Internal frame (3)
Outer lining (4)
Lower press section (5)
Compression section (6)
Lower partition wall (7)
Accessory section (8)
Upper partition wall (9)
Casing (13)
Compression unit (14)
Pre-compression roller (32)
Compression roller (33)
Adjustable block (34)
Bracket (37)
Paddle drive motors (50, 51)
Drive shafts (52, 53)
Coupling parts (54, 55)
Coupling halves (56, 57, 59)
Supply channel (58)
Support column (71)

TECH MECHANICAL ENGINEERING - Preferred Components: At least one of the cleaning fluid devices is provided with a cleaning fluid spray nozzle arranged for automatic introduction through the corresponding connection piece on the compression unit. A drive shaft is provided for detachable connection to the rotary die table of the compression unit for rotation of the die table during cleaning in order to effect axial displacement of the punches. An automatic manipulator is adapted for adjustment of a cam of the compression unit. At least a cam is provided for cooperation with a second end of the punches in order to effect axial displacement of the punches by rotation of the die table. Alternatively, the cleaning station may be for automated cleaning of a compression unit. The cleaning station comprises a cleaning chamber for accommodation of the compression unit during cleaning. The cleaning chamber is provided with cleaning fluid spray nozzle(s). The cleaning station comprises an automatic manipulator for opening at least partially a chamber which includes the compression unit and which, before opening, encloses at least a die opening and its corresponding first punch end. The cleaning chamber is adapted so that the second punch ends are accessible for

actuation from outside the cleaning chamber. An automatic manipulator is provided for opening and/or moving a powder feeding device and/or a tablet discharge device of the compression unit.

POLYMERS - Preferred Components: The releasable conduit connections comprise plastic tubes.

FS CPI

MC CPI: A12-H00H; B11-C05

PLE UPA 20050707
[1.1] 2004 P0000; S9999 S1661;
[1.2] 2004 ND01; Q9999 Q7885-R; Q9999 Q8037 Q7987; Q9999 Q7034-R;

CMC UPB 20050707
M6 *01* R501 R523 R530 R538 R760 M905

L173 ANSWER 6 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 2004-591262 [57] WPIX Full-text

ED 20050531

CR 2003-219332; 2003-719634; 2004-550874; 2005-098345

DNC C2004-214855 [57]

TI An animal feed composition useful as an antibiotic, as growth promoters and feed efficiency promoters in animals comprises improved particle size of chlortetracycline

DC B05; C03; D13; D16; E14

IN WINSTROM W L

PA (PENN-N) PENNFIELD OIL CO

CYC 1

PI US 6773717 B1 20040810 (200457)* EN 21[6]

ADT US 6773717 B1 CIP of US 1999-350474 19990709; US 6773717 B1 Cont of US 2000-587410 20000605; US 6773717 B1 CIP of US 2000-587411 20000605; US 6773717 B1 Provisional US 2000-213424P 20000622; US 6773717 B1 US 2003-390453 20030317

FDT US 6773717 B1 CIP of US 6506402 B; US 6773717 B1 Cont of US 6562615 B

PRAI US 2003-390453 20030317
US 1999-350474 19990709
US 2000-587410 20000605
US 2000-587411 20000605
US 2000-213424P 20000622

IPCR A23K0001-17 [I,A]; A23K0001-17 [I,C]; A23K0001-18 [I,A]; A23K0001-18 [I,C]; C12P0029-00 [I,A]; C12P0029-00 [I,C]

EPC A23K0001-17; A23K0001-18M1; C12P0029-00

NCL NCLM 424/442.000
NCLS 424/116.000; 424/405.000; 424/409.000; 424/410.000; 424/417.000; 424/464.000; 424/489.000; 426/635.000; 514/152.000; 514/153.000

AB US 6773717 B1 UPAB: 20050907

NOVELTY - An animal feed composition comprises improved particle size of chlortetracycline.

DETAILED DESCRIPTION - An animal feed composition (I) comprising improved particle size of chlortetracycline, is prepared by:

(a) providing first and second quantities of fermentation broth (produced by fermentation of an organism producing chlortetracycline and quantities of fermentation broth comprising fermentation solids and liquids), comprising chlortetracycline;

(b) adjusting the pH of the first quantity of fermentation broth to of 7 or greater to produce fermentation broth containing chlortetracycline in the free base form;

(c) lowering the pH of second quantity of fermentation broth to a level sufficient to dissolve the chlortetracycline in second quantity of fermentation broth;

(d) removing solids from pH-adjusted second quantity of fermentation broth and collecting liquid containing dissolved chlortetracycline;

(e) adjusting the pH of liquid containing dissolved chlortetracycline to 7 or greater to produce a suspension of chlortetracycline in the free base form;

(f) mixing fermentation broth containing chlortetracycline in the free base from step (b) and suspension of chlortetracycline in the free base form from step (e);

(g) removing liquids from the mixture of step (f) to produce a fermentation product having a low moisture content containing chlortetracycline in the free base form; and

(h) sizing low moisture content fermentation product to produce a particulate fermentation product containing chlortetracycline in the free base form having a predetermined particle size or range of particle sizes.

ACTIVITY - Anabolic; Antimicrobial; Antibacterial.

No biological data given.

MECHANISM OF ACTION - None given.

USE - (I) is useful as an antibiotic, as growth promoters and feed efficiency promoters in animals such as poultry and livestock.

ADVANTAGE - Solid particulates of (I) have good strength and fracture toughness.

TECH PHARMACEUTICALS - Preferred Method: The ratio of first quantity of fermentation broth to second quantity of fermentation broth is from 1 :10-10:1 (preferably 1:3-3:1). The first quantity of fermentation broth and the second quantity of fermentation broth are from the same or different fermentation batch. The pH of the first quantity of fermentation broth is adjusted to 7.5-8.0 by the addition of aqueous ammonia. The pH of second quantity of fermentation broth is adjusted by adding a mineral acid (oxalic acid, hydrochloric acid or

sulfuric acid) to 4.0 or less (preferably 1.0-1.3). The pH of liquid containing dissolved chlortetracycline is adjusted by the addition of aqueous ammonia to 7.5-8.0. Removal of liquids utilizes at least one of a filter press, centrifugal filter, rotary vacuum filter, oven, tray dryer, tunnel dryer, spray dryer, spray granulator, fluid bed dryer, shelf dryer, drum dryer, rotary dryer, microwave dryer or contact dryer (preferably a filter press, a centrifuge or an oven). The filter cake is dried to a moisture content of 2-12 (preferably 2-6)%. The low moisture content fermentation product comprises chlortetracycline in an amount 30-75 (preferably 44-55)%.

Preferred Composition: The particles are in the form of a powder, meal, pellets, granules or tablets. The composition further comprises blending the particulate chlortetracycline-containing fermentation product with at least one diluent of an edible feed material, a mineral product or an oil.

ABEX ADMINISTRATION - Administration of (I) is oral.

L173 ANSWER 7 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2004-546807 [53] WPIX Full-text
ED 20050531
DNC C2004-200661 [53]
DNN N2004-432369 [53]
TI Seamless capsule for filling food, drink, pharmaceuticals, cosmetics and quasi-drugs, has skin layer containing gelatin, and alpha,alpha-trehalose and/or sucrose
DC B07; D13; D21; P33
IN KATO Y; OKI T; SAITO N; WAKIBUCHI K
PA (HAYB-C) HAYASHIBARA SEIBUTSU KAGAKU; (KOIK-N) KOIKEYA KK
CYC 1
PI JP 2004196706 A 20040715 (200453)* JA 12[0]
ADT JP 2004196706 A JP 2002-366980 20021218
PRAI JP 2002-366980 20021218
IPCR A23L0001-00 [I,A]; A23L0001-00 [I,C]; A61J0003-07 [I,A]; A61J0003-07 [I,C]; A61K0047-26 [I,A]; A61K0047-26 [I,C]; A61K0047-42 [I,A]; A61K0047-42 [I,C]; A61K0008-11 [I,A]; A61K0008-11 [I,C]; A61K0009-48 [I,A]; A61K0009-48 [I,C]
AB JP 2004196706 A UPAB: 20050531
NOVELTY - Seamless capsule has skin layer containing gelatin, and alpha,alpha-trehalose and/or sucrose.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) oral product obtained by filling oral substance or substance to be swallowed such as food, drink, pharmaceuticals, cosmetics or quasi-drugs, in the seamless capsule; and

(2) manufacture of the seamless capsule or oral product by molding aqueous solution containing gelatin, alpha,alpha-trehalose and/or sucrose in the shape of a film and drying.

USE - For filling food, drink, pharmaceuticals, cosmetics and quasi-drugs (claimed).

ADVANTAGE - The seamless capsule provides new food feeling and has good taste, hence easy to masticate. alpha,alpha-trehalose has sweetness lower than sucrose, hence does not produce caries and effectively suppresses flavor of gelatin. The seamless capsule has improved preservability, retained food feeling and skin layer disintegration property for long period of time. Sucrose and/or alpha,alpha-trehalose prevents browning of skin layer by maillard reaction.

TECH ORGANIC CHEMISTRY - Preferred Amount: The seamless capsule contains 0.5-2 mass parts of alpha,alpha-trehalose and/or sucrose with respect to 1 mass part of gelatin. The content ratio between alpha,alpha-trehalose, and alpha,alpha-trehalose and/or sucrose is 30 mass% or more.

Preferred Properties: The skin layer has film thickness of 0.03-0.37 mm.

ABEX EXAMPLE - 15 mass parts of gelatin and 15 mass parts of alpha,alpha-trehalose were dissolved in 70 mass parts of water and heated. Then evacuated with an aspirator, temperature was retained at 75degreesC, and seamless capsule with diameter of 7 mm, coating rate of 10 mass% and filled with mentha oil was produced. The capsule was dried until moisture content was 8 mass%, and seamless capsule filled with mentha oil was obtained. The capsule had good flavor, food quality, disintegrating property and mentha releasing property.

L173 ANSWER 8 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2004-227112 [21] WPIX Full-text
ED 20050528
DNC C2004-089546 [21]
TI Pure, readily digestible sesame seed protein composition, useful as component or additive in human foodstuffs, obtained from defatted sesame seed flour by treatment in aqueous medium
DC D13
IN SIMON CORREA R A
PA (DIPA-N) DIPASA MEXICO SA DE CV
CYC 94
PI WO 2004019694 A1 20040311 (200421)* ES 24[0]
AU 2003208649 A1 20040319 (200462) EN
MX 2002008495 A1 20040301 (200475) ES
ADT WO 2004019694 A1 WO 2003-MX5 20030129; MX 2002008495 A1 MX 2002-8495 20020830; AU 2003208649 A1 AU 2003-208649 20030129

FDT AU 2003208649 A1 Based on WO 2004019694 A
PRAI MX 2002-8495 20020830
IPCR A23J0001-00 [I,C]; A23J0001-14 [I,A]; A23J0003-00 [I,C]; A23J0003-14 [I,A]
EPC A23J0001-14; A23J0003-14
AB WO 2004019694 A1 UPAB: 20050528
NOVELTY - A new sesame seed protein composition (A) consists of pure protein free of the natural chemical impurities found in the seeds and is obtained from defatted sesame seed flour.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the extraction, isolation and purification of sesame seed proteins, involving:

(1) dissolving defatted sesame seed flour in alkali-containing water of pH 9-11 at 15-45degreesC under continuous stirring for 5-120 minutes;

(2) separating the protein solution, having a total solids content of 4-7% and a pH of 9-11, by filtration or centrifugation;

(3) concentrating using ultrafiltration membranes at 25-45degreesC and 20-100 psi, to give a concentrate having a total solids concentration of 12-17% without exceeding 20degrees Brix;

(4) cooling in a heat exchanger to 5-15degreesC; and

(5) neutralizing to pH 6.5-7.5 with acid.

USE - (A) is useful as a protein ingredient and/or additive for various types of human foodstuffs, e.g. dairy, meat or bread products, food supplements or products requiring emulsifying properties.

ADVANTAGE - (A) has good nutritional and functional properties, is readily digestible and is obtainable on an industrial scale by the present process. Sesame seed protein has a good balance of sulfur-containing aminoacids and has 85% of the lysine content in available form.

TECH FOOD - Preferred Product: The defatted sesame seed flour is obtained from seeds from which the cortex has been removed, specifically by chemical or preferably mechanical methods. (A) is obtained in liquid, powder, tablet or pellet form.

Preferred Process: The solution is dried (preferably by spray-drying at 180-260 (especially 70-110)degreesC) to obtain a powder containing at least 90% proteins (based on solids). The solution is prefiltered before concentration. The alkali used in the first stage is calcium hydroxide, ammonium hydroxide, sodium hydroxide (most preferred) or potassium hydroxide. In the first three stages is 1:8-20 and the total solids content is more than 90%. The separation stage is carried out using a filter press, plate centrifuge, rotary vacuum filter, basket centrifuge, decantation centrifuge or dish centrifuge, preferably a centrifuge decanter. The ultrafiltration membrane has a cut-off of 10000 Daltons. Cooling is carried out using a tube or preferably

plate heat exchanger. Neutralization is carried out using phosphoric, acetic, citric, nitric or preferably hydrochloric acid. A variant on the process involves:
(1) dissolving defatted sesame seed flour in alkali-containing water as above;
(2) separating the protein solution as above;
(3) adjusting the pH to 4-5 (i.e. the isoelectric point of the protein) with acid;
(4) separating the precipitate and supernatant by centrifugation;
(5) adjusting the total solids content to 15-20%;
(6) cooling the precipitated proteins in a heat exchanger to 5-15degreesC; and
(7) neutralizing to pH 6.5-7.5 with alkali.

ABEX EXAMPLE - None given in the source material.
FS CPI
MC CPI: D03-H01

L173 ANSWER 9 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2004-088672 [09] WPIX Full-text
ED 20050528
CR 2002-582018; 2002-722083
DNC C2004-036001 [09]
TI Composition useful for the enzymatic hydrolysis of lactose in patients with lactose intolerance, comprises two lactase enzymes having distinct pH maxima
DC B04; D16
IN EISENHARDT P F; SMITH L P
PA (EISE-I) EISENHARDT P F; (MCNI-C) MCNEIL-PPC INC; (SMIT-I) SMITH L P
CYC 1
PI US 20020187139 A1 20021212 (200409)* EN 8[2]
<--
US 6562339 B2 20030513 (200414) EN
<--
ADT US 20020187139 A1 Div Ex US 1995-543975 19951017; US 20020187139 A1 US 2002-139758 20020506
FDT US 20020187139 A1 Div ex US 6410018 B
PRAI US 2002-139758 20020506
US 1995-543975 19951017
IPCR A61K0038-43 [I,C]; A61K0038-47 [I,A]
EPC A61K0038-47
NCL NCLM 424/094.600
NCLS 424/094.610
AB US 20020187139 A1 UPAB: 20050528
NOVELTY - Composition for the enzymatic hydrolysis of lactose, comprising a first active lactase having a first optimum pH range and a second active lactase having a second optimum pH range where the first and second optimum pH rages are different, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) enzymatic hydrolysis of lactose comprising:

(a) hydrolyzing in the intestinal environment having a first pH a first portion of the lactose with a first active lactase having a first optimum pH range which encompasses the first pH; and

(b) hydrolyzing in the intestinal environment having a second pH a second portion of the lactose with a second active lactase having a second optimum pH range, where the first and second pH are of a different magnitude; and

(2) treating or controlling the symptoms of lactose intolerance in humans comprising:

(a) a first lactase having an optimum pH range which encompasses the pH range of the stomach environment; and

(b) a second lactase having an optimum pH range which encompasses the pH range of the intestinal environment.

ACTIVITY - Gastrointestinal-Gen. No biological data given.

MECHANISM OF ACTION - Enzymatic hydrolysis.

USE - For the treatment or control of symptoms associated with lactose intolerance in humans (claimed).

ADVANTAGE - The composition in addition to hydrolyzing lactose under the normal acidic conditions found in a healthy stomach also has enzymatic activity in the more neutral environment of the intestines and in the stomachs of the elderly suffering from achlorhydria and users of H2 blockers.

TECH BIOTECHNOLOGY - The composition further comprises an orally administrable environment. The optimum pH range of hte first lactase encompasses the pH range of 3.0 to 6.0, the second lactase encompasses the pH range 6.0 to 8.0. The first lactase is a bacterial lactase derived from Thermus aquaticus or a fungal lactase derived form the genera of fungi selected from the group consisting of Aspergillus, Mucor, Fusarium, Scopulariopsis, Alternaria and/or Curvularia. Preferably the lactase is derived from Aspergillus oryzae, A. niger, Fusarium moniliforme, Scopulariopsis, Mucor pucillus, Alternaria alternara and Curvularia inaequalic, and especially A. oryzae, A. niger and M. pucillus. The second lactase is derived from Kluyveromyces, Bacillus circulans, Lactobacillus bulgaricus, Bacillus sp., Leuconostoc citrovorum, B. stearothermophilus and Streptococcus thermophilus. The composition especially comprises A. oryzae and A. niger as the first lactase and Kluyveromyces lactis as the second. The second lactase is enterically coated.

ABEX ADMINISTRATION - The composition is in a unit dosage form comprising an amount of the first lactase equivalent to about 3000 to about 6000 FCC Lac U and an amount of the second lactase equivalent to about 7000 to about 35,000 neutral lactase units. The composition is for oral administration prior to or concurrently with

the ingestion of lactose-containing food. (All claimed). The composition is delivered in a caplet each containing 770 mg of the active composition and an adult human would generally consume two or more caplets per dose.

EXAMPLE - A preparative example is included for a caplet form of the composition containing an enzyme derived from Aspergillus oryzae as the first lactase enzyme having activity in the acid region and an enzyme derived from Kluyveromyces lactis as the second lactase having activity in the neutral region: Lactase powder was derived from K. lactis was coated with an enteric suspension comprising cellulose acetate phthalate NF (11% by Wt.) (AQUATERIC powder), triacetin USP (3.9% by Wt.), polysorbate 80 NF (TWEEN 80) (0.1% by Wt.) and purified water (85% by Wt.). The enzyme powder was charged into a Wurster fluidized bed coating apparatus and fluidized by a flow of warm air. The enzyme powder attained a product temperature of 28-37degrees C. The enteric suspension was then sprayed onto the fluidized enzyme particles at a rate of 9 mL/min. until the coated enzyme particles contained an approximately 13% by weight of the enteric coating. The enterically coated enzyme particles were combined with the following ingredients to produce the caplet: Enterically coated lactase (K. Lactis) (517.6 mg/caplet; 75% W/W), lactase powder (A. oryzae) (15.0 mg/caplet; 2.2% W/W), microcrystalline cellulose, NF (153.4 mg/caplet; 22.2% W/W) and magnesium stearate, NF (4.0 mg/caplet; 0.6% W/W). The enterically coated lactase (K. lactis), lactase derived from A. oryzae and microcrystalline cellulose were dry blended in a twin shell blender for 20 min. The magnesium stearate was added to the mixture and blended for an additional 5 min. The mixture was then compressed into a caplet on a rotary tablet press.

IT UPIT 20050528
200757-CL

FS CPI

MC CPI: B04-F09; B04-F10; B04-L05; B07-A02B; B11-A01; B12-M05; B12-M10B; B12-M11B; B12-M11C; B14-E10; D05-C03C; D05-H08

CMC UPB 20050528
M1 *01* M417 M423 M431 M782 N131 N132 N134 N136 P712 Q233 M905
DCN: RA00GT-K RA00GT-M RA00GT-T
DCR: 200757-K 200757-M 200757-T 200799-K 200799-M 200799-T

L173 ANSWER 10 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 2004-081840 [08] WPIX Full-text

ED 20050706

DNC C2004-033608 [08]

TI Composition useful in the treatment of e.g. post-surgery pain, chronic pain in the spine and acute osteoporosis comprises mixture

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     of active substance and adjuvants
DC   A96; B02; B07
IN   GATTNAR O; HUBINOVA V; KORMANOVA V; LEHOCKY M; RAZUS L; VARGA I;
     VARGA N
PA   (SLOV-N) SLOVAKOFARMA AS; (ZENT-N) ZENTIVA AS
CYC  101
PI   WO 2003086365   A1 20031023 (200408)* EN  8[0]
     <--
     SK 2002000501   A3 20031104 (200408)  SK
     <--
     AU 2003219641   A1 20031027 (200436)  EN
     <--
     EP 1494656      A1 20050112 (200504)  EN
     CZ 2004001054   A3 20050112 (200508)  CS
     NO 2004004502   A  20041026 (200519)  NO
     HU 2005000438   A2 20050829 (200580)  HU
     EP 1494656      B1 20080618 (200842)  EN
     DE 60321672     E  20080731 (200853)  DE
ADT  WO 2003086365 A1 WO 2003-SK8 20030410; SK 2002000501 A3
     SK 2002-501 20020412; AU 2003219641 A1 AU 2003-219641
     20030410; EP 1494656 A1 EP 2003-715908 20030410; EP
     1494656 B1 EP 2003-715908 20030410; EP 1494656 A1 WO
     2003-SK8 20030410; CZ 2004001054 A3 WO 2003-SK8
     20030410; NO 2004004502 A WO 2003-SK8 20030410; HU
     2005000438 A2 WO 2003-SK8 20030410; EP 1494656 B1 WO
     2003-SK8 20030410; CZ 2004001054 A3 CZ 2004-1054
     20030410; NO 2004004502 A NO 2004-4502 20041021; HU 2005000438
     A2 HU 2005-438 20030410; DE 60321672 E DE
     2003-60321672 20030410; DE 60321672 E EP 2003-715908
     20030410; DE 60321672 E WO 2003-SK8 20030410
FDT  AU 2003219641   A1 Based on WO 2003086365   A; EP 1494656      A1
     Based on WO 2003086365   A; CZ 2004001054   A3 Based on WO
     2003086365   A; HU 2005000438   A2 Based on WO 2003086365   A; EP
     1494656      B1 Based on WO 2003086365   A; DE 60321672     E Based
     on EP 1494656      A; DE 60321672     E Based on WO 2003086365   A
PRAI SK 2002-501          20020412
IC   ICM A61K009-22
     ICS A61K031-485
IPCI A61K0031-485 [I,A]; A61K0031-485 [I,A]; A61K0031-485 [I,C];
     A61K0031-485 [I,C]; A61K0009-22 [I,A]; A61K0009-22 [I,A];
     A61K0009-22 [I,C]; A61K0009-22 [I,C]
IPCR A61K0031-485 [I,A]; A61K0031-485 [I,C]; A61K0009-20 [I,A];
     A61K0009-20 [I,C]; A61K0009-22 [I,A]; A61K0009-22 [I,C]
EPC  A61K0031-485; A61K0009-20H2; A61K0009-20H4
ICO  K61K0009:20H6B; K61K0009:20P
AB   WO 2003086365 A1   UPAB: 20060203
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NOVELTY - A composition (I) comprises a mixture of opioid active substance (A) and adjuvants. One of the adjuvant (B) ensures controlled release and another adjuvant (C) is water-insoluble filler. The release profile of (A) is optionally set up by the ratio of disintegrate from pressings and the primary granulated mixture.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for preparation of (I) involving:

(1) blending (A) with a micronized ester of glycerol and behenic acid with calcium phosphate dihydrate; and

(2) moistening the mixture with a solution of a copolymer of vinylpyrrolidone and vinylacetate in a ratio of 6:4 having relative molecular weight (45000 - 70000) in a mixture of ethyl alcohol and water to give agglomerated mixture.

ACTIVITY - Analgesic; Osteopathic; Antiarthritic.

MECHANISM OF ACTION - None given.

USE - In the treatment of moderately strong to strong pain e.g. post-surgery pain, post-injury pain, chronic pain in the spine, severe arthritis, acute osteoporosis, neurogenic pain, pain related to cancer and other pains.

ADVANTAGE - The composition allows controlled release of opioid active substance. (I) can be prepared using a more simple and less demanding technological process that does not require any special manufacturing device for the granulation with supply of heat energy and without need of incorporating auxiliary materials influencing release of the agent in the molten state. The composition complies with the requirements of the release and does not require any additional treatment such as coating with a film. The composition can be pressed with any required therapeutic content of the active substance and with any shape maintaining the release profile. The composition is chemically and physically stable for sufficient period of time and can be inserted into commonly used pharmaceutical packages without any problems.

TECH ORGANIC CHEMISTRY - Preferred Process: The agglomerate is either box dried, vacuum dried, fluidization dried or microwave dried (preferably fluidization dried) until the residual humidity is (0.1 - 2, preferably 0.5 - 1.5) wt.%. The temperature of the product during drying is 35 - 42 (preferably 39 - 41)degreesC. The dried agglomerate is resized to a particle size to match the tablet compressing process by the oscillation method through a sieve having size of opening 0.65 - 8 (preferably 0.7) mm. The micronized sodium salt of the ester of fumaric acid and stearyl alcohol is mixed in an amount of (0.2 - 3, preferably 0.8 - 1.5) wt.% having a particle size (up to 10, preferably up to 8) micro m. The mixture is compressed into tablets having required content of (A) and having fracture resistance (40 - 110, preferably 60 - 85) N. To achieve the required profile of release of (A) from the tablet, the finished mixture (1 - 99, preferably 65 - 85) wt.% is compressed into

pressings of any shape and weight. The pressings are disintegrated by oscillation method and the disintegrate is thoroughly homogenized with previously not compressed or not disintegrated residue of the prepared lot.
Preferred Composition: (I) comprises (wt.%): (A) (25 - 40, preferably 27 - 35), (C) (preferably calcium phosphate dihydrate (10 - 60, preferably 15 - 50)), (B) (preferably glyceryl ester of behenic acid (10 - 60, preferably 20 - 50)) having particle size 1 - 100 micro m (preferably 90% of the particles is of size 1.5 - 60 micro m), a copolymer of vinylpyrrolidone and vinyl acetate in a weight ratio of 6:4 (1 - 6, preferably 1.5 - 4) having relative molecular weight of 45000 - 70000 and micronized sodium salt of the ester of fumaric acid with stearyl alcohol (0.2 - 3, preferably 0.8 - 1.5) having particle size (up to 10, preferably 8) mum.
Preferred Components: The mixture of ethyl alcohol and water, in which the co-polymer of vinylpyrrolidone and vinyl acetate is dissolved at laboratory temperature comprises ethyl alcohol (10 - 80 preferably 25 - 75) wt.%. (B) is a micronized ester of glycerol with higher fatty acids (preferably micronized ester of glycerol with behenic acid). (A) is dihydrocodeine and/or its salt.
INORGANIC CHEMISTRY - Preferred Components: (C) is at least one alkali salt of phosphoric acid (preferably calcium phosphate dihydrate).

ABEX ADMINISTRATION - The composition is administered orally (claimed) in the form of a tablet. No dosage given.
EXAMPLE - Dihydrocodeine tartrate (33.33%) was blended with micronized glyceryl ester of behenic acid (46.66%) having particle size (1 - 60) micro m and with calcium phosphate dihydrate (16.39%) in a granulator. The blended mixture was moistened gradually with a solution of vinylpyrrolidone-vinylacetate co-polymer (2.51%) in a ratio of 6:4 in a mixture of 48% ethyl alcohol-water until agglomerate forms. The agglomerate was transferred to the vessel of a device for fluidization drying and was dried under moderate fluidization at 55 degrees C until the temperature was 40 degrees C which indicated completion of drying process. The dried out granulate was subjected to resizing and was homogenized in a dry homogenizer device with sodium stearyl fumarate (1.11%). The mixture was then compressed in rotary tablet forming machine into tablet. The tablet was then subjected to dissolution test. The dissolution rate of the tablet was determined at 1, 2 and 4 hours and was found to be 36.9%, 64.6% and 100% respectively.

L173 ANSWER 11 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2004-060033 [06] WPIX Full-text
ED 20050527
CR 2003-333267; 2003-333268; 2003-333269; 2003-363185; 2003-363254;

2003-371873; 2003-371874; 2003-371958; 2003-371959; 2003-371972; 2003-381522; 2003-381596; 2003-541394; 2003-541395; 2003-541396; 2003-597868; 2003-607585; 2004-070103; 2004-070359; 2004-097315; 2004-097832; 2004-178823; 2004-224095; 2004-305108; 2004-375416; 2004-389327; 2004-542579; 2004-642113; 2005-030193; 2005-434299; 2005-434357; 2005-505288; 2007-070604

DNC C2004-024834 [06]

DNN N2004-048534 [06]

TI Transfer apparatus for substrates, e.g. tablets, includes cam track defining path from first substrate receiving station, passing through second substrate receiving station and to substrate transfer station

DC B07; Q35

IN SOWDEN H S

PA (SOWD-I) SOWDEN H S

CYC 1

PI US 20030217908 A1 20031127 (200406)* EN 9[8]
<--
US 6880694 B2 20050419 (200527) EN

ADT US 20030217908 A1 CIP of US 2001-967414 20010928; US 20030217908 A1 US 2003-393609 20030321; US 6880694 B2 CIP of US 2001-967414 20010928; US 6880694 B2 US 2003-393609 20030321

FDT US 6880694 B2 CIP of US 6742646 B

PRAI US 2003-393609 20030321
US 2001-967414 20010928

IPCR A23G0003-00 [I,A]; A23G0003-00 [I,C]; A23G0003-02 [I,C]; A23G0003-04 [I,A]; A23G0003-34 [I,C]; A23G0003-36 [I,A]; A61J0003-10 [I,A]; A61J0003-10 [I,C]; A61K0031-167 [I,A]; A61K0031-167 [I,C]; A61K0047-10 [I,A]; A61K0047-10 [I,C]; A61K0047-12 [I,A]; A61K0047-12 [I,C]; A61K0047-34 [I,A]; A61K0047-34 [I,C]; A61K0047-36 [I,A]; A61K0047-36 [I,C]; A61K0047-42 [I,A]; A61K0047-42 [I,C]; A61K0009-00 [I,A]; A61K0009-00 [I,C]; A61K0009-20 [I,A]; A61K0009-20 [I,C]; A61K0009-24 [I,A]; A61K0009-24 [I,C]; A61K0009-28 [I,A]; A61K0009-28 [I,C]; A61K0009-30 [I,A]; A61K0009-30 [I,C]; A61K0009-40 [I,A]; A61K0009-50 [N,A]; A61K0009-50 [N,C]; A61P0029-00 [I,A]; A61P0029-00 [I,C]; B30B0011-02 [I,C]; B30B0011-08 [I,A]

EPC A23G0003-04; A23G0003-36M4; A61J0003-10; B30B0011-08

ICO K61K0009:28H6D; K61K0009:28H6H; K61K0009:28P

NCL NCLM 198/377.040
NCLS 198/471.100; 198/803.150

AB US 20030217908 A1 UPAB: 20060120
NOVELTY - Transfer apparatus (12) comprises a flexible conveyor (13); transfer units (14) mounted to the conveyor, in which each transfer unit is adapted to hold first and second substrates; a cam track defining a path from a first substrate receiving station (18a), passing through a second substrate receiving station (18b) and to a

substrate transfer station (19); and driving mechanism for driving the conveyor along the cam track.

USE - For use in transferring substrates, e.g. tablets (claimed) from rotary double-sided tablet press (1) to a second location.

ADVANTAGE - The invention effectively transfer the tablets on a continuous basis. The retainers coupled with the path followed by the cam track allow the transfer unit to pick up one substrate at a time continuously.

DESCRIPTION OF DRAWINGS - The figure depicts a transfer apparatus coupled with a tablet press.

Transfer apparatus (12)
Conveyor (13)
Transfer units (14)
First substrate receiving station (18a)
Second substrate receiving station (18b)
Substrate transfer station (19)

TECH INSTRUMENTATION AND TESTING - Preferred Apparatus: The transfer units are mounted to the conveyor in a cantilever configuration. Each transfer unit has first and second retainers positioned on either side of the conveyor and having segmented fingers. The retainers are located on sides in each transfer unit and adapted for holding respective substrate. The path positions of the conveyor are on the outside of the first and second substrate receiving stations. The apparatus includes a vacuum for applying a vacuum to the substrates while they are held by the transfer units. The transfer units are mounted to the conveyor so that they are capable of rotating while traveling along the cam track. A rotatable actuator arm is linked to transfer units.

POLYMERS - Preferred Material: The retainers are made of elastomeric material.

IT UPIT 20060120
184613-CL 184613-USE

FS CPI; GMPI

MC CPI: B04-C03; B11-C03; B11-C05; B11-C06

CMC UPB 20060120
M1 *01* M417 M423 M424 M740 M781 N101 M905
DCN: RA00I9-K RA00I9-U
DCR: 184613-K 184613-U
M6 *02* R170 R501 R530 R760 M905

L173 ANSWER 12 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 2003-479402 [45] WPIX Full-text

ED 20050530

CR 2002-582018; 2002-722083

DNC C2003-128017 [45]

TI Lactose enzymatic hydrolyzing composition for treating or

controlling symptoms of lactose intolerance in humans, comprises two active lactase having different optimum pH ranges

DC B04; D16

IN EISENHARDT P F; SMITH L P

PA (EISE-I) EISENHARDT P F; (MCNI-C) MCNEIL-PPC INC; (SMIT-I) SMITH L P

CYC 1

PI US 20020172669 A1 20021121 (200345)* EN 8[2]
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US 6562338 B2 20030513 (200345) EN
<--

ADT US 20020172669 A1 Div Ex US 1995-421825 19950606; US 20020172669 A1 US 2002-139493 20020506; US 6562338 B2 Div Ex US 1995-421825 19950606; US 6562338 B2 US 2002-139493 20020506

FDT US 6562338 B2 Div ex US 6428786 B

PRAI US 2002-139493 20020506
US 1995-421825 19950606

IPCR A61K0038-43 [I,C]; A61K0038-47 [I,A]

EPC A61K0038-47

NCL NCLM 424/094.600
NCLS 424/094.610

AB US 20020172669 A1 UPAB: 20050530
NOVELTY - A lactose enzymatic hydrolyzing composition (I) comprising first, active lactase having a first optimum pH range, and second, active lactase having a second optimum pH range, is new. The two optimum pH ranges are different.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the enzymatic hydrolysis of lactose in mammals comprising hydrolyzing in the stomach environment having a first pH a first portion of lactose with first, active lactase having a first optimum pH range which includes the first pH, and hydrolyzing in the intestinal environment having a second pH a second portion of the lactose with a second, active lactase having a second optimum pH range which includes the second pH.

ACTIVITY - None given.

No suitable data given.

MECHANISM OF ACTION - None given.

USE - (I) is useful for treating or controlling the symptoms of lactose intolerance, in humans.

ADVANTAGE - (I) includes lactase having optimum pH ranges that enable the composition to enzymatically hydrolyze lactose in environment having different or varying pHs.

TECH BIOTECHNOLOGY - Preferred Compositions: The composition further comprising a carrier.

Preferred Components: The first, active lactase is a fungal lactase or bacterial lactase derived from Thermus aquaticus. The first, active lactase is enterically coated. The second, active lactase is

a yeast or bacterial lactase. The first lactase is derived from the genera of fungi, which can be Aspergillus, Mucor, Fusarium, Scopulariopsis, or Alternaria, and Curvularia. The first lactase is derived from a fungi, which can be Fusarium moniliforme, Scopulariopsis, Alternaria alternara or Curvularia inaegualic, or preferably Aspergillus oryzae, Aspergillus niger, or Mucor pucillus. The second lactase is Kluyveromyces, Lactobacillus, Bacillus, or Streptococcus. The second lactase is derived from Kluyveromyces lactis, Kluyveromyces fragilis, Lactobacillus thermophilus, Bacillus circulans, Lactobacillus bulgaricus, Bacillus sp., Leuconostoc citrovorum, Bacillus stearothermophilus, or Streptococcus thermophilus. The second lactase is Kluyveromyces lactis. Preferred Parameters: The first optimum pH range is 3-6, and the second optimum pH range of 6-8. The unit dosage of the first lactase is 3000-6000 FCC Lac U and the unit dosage of the second lactase is 7000-35,000 neutral lactase units.

PHARMACEUTICALS - Preferred Process: The composition is administered prior to or concurrently with the ingestion of lactose-containing food or composition.

ABEX ADMINISTRATION - The composition is administered to adult human at at least2 caplets (770 mg) per dose before or concurrently with the ingestion of lactose-containing food or composition.

EXAMPLE - A formulation for preparing a caplet form of the inventive composition contained enzyme derived from Aspergillus oryzae as first enzyme having activity in acid region and enzyme derived from Kluyveromyces lactis as second lactase having activity in the neutral region. The lactase powder derived from K. lactis was coated and worked up to attain product temperature of 28-337degreesC. The enteric suspension was then sprayed to fluidized enzyme particles at 9 ml/min until the coated enzyme particles contain approximately13 wt.% of entering coating. The coated lactase (K. lactis) (75 wt.%), lactase derived from A. oryzae (2.2 wt.%), and microcrystalline cellulose (22.2 wt.%) were dry blended for 20 minutes. A magnesium stearate (0.6 wt.%) was added to the mixture, which was compressed into a caplet on rotary press.

IT UPIT 20050530
184598-CL 184598-NEW

FS CPI

MC CPI: B04-F09; B04-F10; B04-L05B; D05-A02C; D05-C03C

CMC UPB 20050530
M1 *01* M417 M423 M710 M730 Q233 M905
DCN: RA00GC-N RA00GC-S
DCR: 184598-N 184598-S

L173 ANSWER 13 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 2003-354626 [33] WPIX Full-text

ED 20050529
DNC C2003-093526 [33]
TI Rapidly disintegrating tablets with high content of plant extract, especially St. John's wort extract, obtained using highly dispersed silica as parting agent and sodium bicarbonate-based disintegrant mixture
DC A96; B07
IN KROLL U; KUPER W
PA (KROL-I) KROLL U; (KUPE-I) KUPER W; (STEA-C) STEIGERWALD ARZNEIMITTELWERK; (STEA-C) STEIGERWALD ARZNEIMITTELWERK GMBH
CYC 99
PI WO 2003026620 A1 20030403 (200333)* DE 15[0]
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DE 10144108 A1 20030430 (200336) DE
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EP 1349543 A1 20031008 (200370) DE
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HU 2003002459 A2 20031128 (200405) HU
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US 20040067265 A1 20040408 (200426) EN
KR 2004029319 A 20040406 (200451) KO
EP 1349543 B1 20040915 (200460) DE
AU 2002325796 A1 20030407 (200461) EN
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DE 50201005 G 20041021 (200469) DE
AU 2002325796 B2 20041118 (200504) EN
JP 2005502729 W 20050127 (200510) JA 21
ES 2227482 T3 20050401 (200524) ES
RU 2287338 C2 20061120 (200677) RU
US 7374784 B2 20080520 (200843) EN
ADT WO 2003026620 A1 WO 2002-DE2634 20020715; DE 10144108 A1 DE 2001-10144108 20010903; AU 2002325796 A1 AU 2002-325796 20020715; AU 2002325796 B2 AU 2002-325796 20020715; DE 50201005 G DE 2002-50201005 20020715; EP 1349543 A1 EP 2002-760103 20020715; EP 1349543 B1 EP 2002-760103 20020715; DE 50201005 G EP 2002-760103 20020715; ES 2227482 T3 EP 2002-760103 20020715; EP 1349543 A1 WO 2002-DE2634 20020715; HU 2003002459 A2 WO 2002-DE2634 20020715; US 20040067265 A1 WO 2002-DE2634 20020715; EP 1349543 B1 WO 2002-DE2634 20020715; DE 50201005 G WO 2002-DE2634 20020715; JP 2005502729 W WO 2002-DE2634 20020715; RU 2287338 C2 WO 2002-DE2634 20020715; HU 2003002459 A2 HU 2003-2459 20020715; JP 2005502729 W JP 2003-530257 20020715; RU 2287338 C2 RU 2003-120511 20020715; KR 2004029319 A KR 2003-709377 20030714; US 20040067265 A1 US 2003-250547 20031124; US 7374784 B2 WO 2002-DE2634

20020715; US 7374784 B2 US 2003-250547 20031124

FDT AU 2002325796 B2 Previous Publ AU 2002325796 A; DE 50201005 G Based on EP 1349543 A; ES 2227482 T3 Based on EP 1349543 A; EP 1349543 A1 Based on WO 2003026620 A; HU 2003002459 A2 Based on WO 2003026620 A; EP 1349543 B1 Based on WO 2003026620 A; AU 2002325796 A1 Based on WO 2003026620 A; DE 50201005 G Based on WO 2003026620 A; AU 2002325796 B2 Based on WO 2003026620 A; JP 2005502729 W Based on WO 2003026620 A; RU 2287338 C2 Based on WO 2003026620 A; US 7374784 B2 Based on WO 2003026620 A

PRAI DE 2001-10144108 20010903

IC ICM A61K035-78; A61K009-20
ICS A61K047-04; A61K047-12; A61K047-32; A61K047-36; A61K047-38; A61K009-26

IPCI A61K0036-00 [I,A]; A61K0036-00 [I,C]; A61K0036-185 [I,C]; A61K0036-185 [I,C]; A61K0036-38 [I,A]; A61K0036-38 [I,A]; A61K0009-20 [I,A]; A61K0009-20 [I,C]

IPCR A61K0036-00 [I,A]; A61K0036-00 [I,C]; A61K0036-18 [I,A]; A61K0036-18 [I,C]; A61K0036-185 [I,C]; A61K0036-38 [I,A]; A61K0047-02 [I,C]; A61K0047-04 [I,A]; A61K0047-12 [I,A]; A61K0047-12 [I,C]; A61K0047-32 [I,A]; A61K0047-32 [I,C]; A61K0047-36 [I,A]; A61K0047-36 [I,C]; A61K0047-38 [I,A]; A61K0047-38 [I,C]; A61K0009-20 [I,A]; A61K0009-20 [I,C]; A61K0009-26 [I,A]; A61K0009-26 [I,C]

EPC A61K0009-20K2; A61K0009-20P

NCL NCLM 424/725.000
NCLS 264/109.000; 424/730.000

AB WO 2003026620 A1 UPAB: 20050903

NOVELTY - Production of tablets containing plant extracts (A) involves compacting and granulating a mixture of dry (A) and auxiliaries then pressing the compacted particles (masked by moisture protectants, surface smoothing agents parting agents and other auxiliaries) into tablets.

DETAILED DESCRIPTION - Production of tablets containing plant extracts (A) involves compacting and granulating a mixture of dry (A) and auxiliaries then pressing the compacted particles (masked by moisture protectants, surface smoothing agents parting agents and other auxiliaries) into tablets, in which:

(a) the tablets are compacted in the sole presence of highly dispersed silica (acting as parting agent);

(b) further processing is carried out using compacted particles with a specific size and size distribution to give a compacted material with low overall specific surface; and

(c) the compacted material is additionally coated with a disintegrant combination of sodium bicarbonate and smaller amounts of two other disintegrants.

USE - (A) is especially St. John's wort extract (A') (claimed).

ADVANTAGE - The process provides tablets having a very high (A) content, a low adjuvant content and a high disintegration and release rate. Typically tablets of readily ingestible size containing 900 mg of (A') can be produced. Problems due to moisture, separation and decomposition during tableting are eliminated.

TECH PHARMACEUTICALS - Preferred Process: (A) is in the form of a dry extract obtained by vacuum drying. The amount of silica added before compacting is 1%. The particles used in step (b) have a size of ca. 125-1000 microm (especially with a size distribution of 99% less than 1000 microm, at least 90% less than 710 microm, 40-60% less than 500 microm, 30-60% less than 250 microm and at most 40% less than 125 microm); and have (on the basis of the particle size distribution) an obtainable apparent density of 0.63-8.0 g/ml and a tamped density of 0.73-0.85 g/ml. The content of sodium bicarbonate (as disintegrant) is 5-15% and the content of each of the other two disintegrants is 0.5-5%. Magnesium stearate is added as further auxiliary. The masking auxiliaries for surface smoothing and moisture protection are talc and titanium dioxide.

POLYMERS - Preferred Materials: The additional disintegrants preferably consist of croscarmellose sodium and carboxymethyl starch-sodium; more generally starch derivatives, cellulose compounds or polyvinyl pyrrolidone may be used.

ABEX EXAMPLE - A liquid, aqueous ethanolic extract of St. John's wort buds and flowers was filtered, concentrated to ca. 60% by drying under reduced pressure at 40-60 degrees C, sterilized by heating for 15 seconds at 140 degrees C and dried on a belt at 30 - 60 degrees C under reduced pressure. The dry extract was mixed with ca. 1% highly dispersed silica (such that the extract particles were coated with the silica), then compacted by pressing, comminuted in a drum mixer and sieved to give a powder with a size distribution of 99% less than 1000 microm, at least 90% less than 710 microm, 40-60% less than 500 microm, 30-60% less than 250 microm and at most 40% less than 125 microm, an obtainable apparent density of 0.63-8.0 g/ml and a tamped density of 0.73-0.85 g/ml. The particles were masked with titanium dioxide, talc and magnesium stearate; coated with a disintegrant combination of sodium bicarbonate, croscarmellose sodium and carboxymethyl starch-sodium; and pressed to give tablet cores weighing 1090 mg, containing 900 mg of the plant extract and having a width of 9.5 mm, a length of 20.5 mm and a height of 6.6 mm. The cores were covered with pre-coating lacquer then with a colored lacquer.

L173 ANSWER 14 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2003-300150 [29] WPIX Full-text
ED 20050528
CR 2004-765414

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DNN  N2003-238888 [29]
TI   Rotary tablet press used in
     pharmaceutical industry, has detachable compression unit with die
     openings, punch lower ends, feeding device, and tablet
     discharge device that are enclosed
DC   P71
IN   BOECKX J; CHRISTIAENS D; VAN ZEGBROECK A; VOGELEER J; ZEGBROECK A V
PA   (COUR-N) COURTOY NV
CYC  96
PI   US 20030042639  A1 20030306 (200329)* EN  18[9]
     <--
     WO 2003020499   A1 20030313 (200341)  EN
     <--
     US 6676863      B2 20040113 (200405)  EN
     EP 1423260      A1 20040602 (200436)  EN
     AU 2001286137   A1 20030318 (200452)  EN
     <--
     JP 2005501724   W  20050120 (200508)  JA  76
     CN 1545445      A  20041110 (200515)  ZH
     RU 2266822      C2 20051227 (200603)  RU
     CN 1260057      C  20060621 (200674)  ZH
     EP 1423260      B1 20070124 (200710)  EN
     DE 60126355     E  20070315 (200726)  DE
     ES 2280396      T3 20070916 (200763)# ES
     DE 60126355     T2 20071031 (200774)  DE
ADT  US 20030042639 A1 US 2001-960739 20010924; AU 2001286137
     A1 AU 2001-286137 20010905; CN 1545445 A CN
     2001-823602 20010905; CN 1260057 C CN 2001-823602
     20010905; DE 60126355 E DE 2001-626355 20010905; EP
     1423260 A1 EP 2001-965500 20010905; EP 1423260 B1 EP
     2001-965500 20010905; DE 60126355 E EP 2001-965500
     20010905; ES 2280396 T3 EP 2001-965500 20010905; WO
     2003020499 A1 WO 2001-IB1631 20010905; EP 1423260 A1
     WO 2001-IB1631 20010905; AU 2001286137 A1 WO
     2001-IB1631 20010905; JP 2005501724 W WO 2001-IB1631
     20010905; CN 1545445 A WO 2001-IB1631 20010905; RU
     2266822 C2 WO 2001-IB1631 20010905; CN 1260057 C WO
     2001-IB1631 20010905; EP 1423260 B1 WO 2001-IB1631
     20010905; DE 60126355 E WO 2001-IB1631 20010905; JP
     2005501724 W JP 2003-524790 20010905; RU 2266822 C2
     RU 2004-110034 20010905; DE 60126355 T2 DE 2001-626355
     20010905; DE 60126355 T2 EP 2001-965500 20010905; DE
     60126355 T2 WO 2001-IB1631 20010905
FDT  DE 60126355     E Based on EP 1423260      A; ES 2280396      T3
     Based on EP 1423260      A; EP 1423260      A1 Based on WO
     2003020499   A; AU 2001286137   A1 Based on WO 2003020499   A; JP
     2005501724   W Based on WO 2003020499   A; RU 2266822      C2 Based
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on WO 2003020499 A; EP 1423260 B1 Based on WO 2003020499 A; DE 60126355 E Based on WO 2003020499 A; DE 60126355 T2 Based on EP 1423260 A; DE 60126355 T2 Based on WO 2003020499 A

PRAI WO 2001-IB1631 20010905

IC ICM B30B011-08

IPCI B30B0011-02 [I,C]; B30B0011-02 [I,C]; B30B0011-02 [I,C]; B30B0011-08 [I,A]; B30B0011-08 [I,A]; B30B0015-00 [I,A]; B30B0015-00 [I,A]; B30B0015-00 [I,C]; B30B0015-00 [I,C]

IPCR B30B0011-02 [I,C]; B30B0011-08 [I,A]; B30B0015-00 [I,A]; B30B0015-00 [I,C]; B30B0015-32 [I,A]; B30B0015-32 [I,C]

EPC B30B0011-08; B30B0015-00C; B30B0015-00M; B30B0015-32

NCL NCLM 264/039.000
NCLS 264/109.000; 425/193.000; 425/225.000; 425/261.000; 425/348.00R; 425/351.000

AB US 20030042639 A1 UPAB: 20060119

NOVELTY - The press has a detachable compression unit (14) enclosed in a housing and which includes a die table (15), punches (17,18), a feeding device, a table discharge device. Dies (16) are installed at the die table circumference and receive the ends (21,22) of the punches. The die openings, the punch lower ends, the feeding device, and the tablet discharge device are enclosed.

DETAILED DESCRIPTION - The punches are reciprocated with cams (25,26). The feeding device leads powder material into the dies and is connected to an inlet selectively coupled to an external supply channel. The tablet discharge device removes compressed materials in the form of tablets from within the dies to an outlet. The die table is rotated by a drive shaft. INDEPENDENT CLAIMS are also included for the following:

(a) a compression unit for attachment to press housing;
(b) a cleaning station for cleaning compression unit;
(c) a tablet manufacturing method; and
(d) a compression unit cleaning method.

USE - Used in pharmaceutical industry in manufacture of medicine tablets. Also for manufacturing of e.g. vitamin, pet food, detergent, explosive, ceramics, batteries, balls, bearings, nuclear fuels.

ADVANTAGE - Simplifies and expedites cleaning of tablet press between batches, while reducing contamination at surrounding environment and reducing exposure of personnel to hazardous products. Reduces downtime of rotary tablet press.

DESCRIPTION OF DRAWINGS - The figure shows the sectional view of the compression unit.

Detachable compression unit (14)
Die table (15)
Dies (16)
Punches (17,18)

Ends (21,22)
Cams (25,26)
FS GMPI

L173 ANSWER 15 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2002-444436 [47] WPIX Full-text
ED 20050706
DNC C2002-126598 [47]
TI Pharmaceutical composition for treating bacterial infection comprises an erythromycin derivative and at least one of long chain hydrocarbon, long chain carboxylic acid or ester and long chain alcohol
DC B03; B07
IN RUDNIC E M; TREACY D J; WASSINK S E
PA (ADVA-N) ADVANCIS PHARM
CYC 93
PI WO 2002038577 A2 20020516 (200247)* EN 11[0]
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AU 2002039232 A 20020521 (200260) EN
<--
EP 1333807 A2 20030813 (200355) EN
<--
JP 2004528272 W 20040916 (200461) JA 22
MX 2003003146 A1 20050101 (200564) ES
ADT WO 2002038577 A2 WO 2001-US32055 20011012; EP 1333807 A2 EP 2001-986972 20011012; EP 1333807 A2 WO 2001-US32055 20011012; JP 2004528272 W WO 2001-US32055 20011012; MX 2003003146 A1 WO 2001-US32055 20011012; AU 2002039232 A AU 2002-39232 20011012; JP 2004528272 W JP 2002-541109 20011012; MX 2003003146 A1 MX 2003-3146 20030410
FDT AU 2002039232 A Based on WO 2002038577 A; EP 1333807 A2 Based on WO 2002038577 A; JP 2004528272 W Based on WO 2002038577 A; MX 2003003146 A1 Based on WO 2002038577 A
PRAI US 2000-689988 20001013
IC ICM A61K031-7048
IPCR A61K0031-7042 [I,C]; A61K0031-7048 [I,A]; A61K0047-02 [I,A]; A61K0047-02 [I,C]; A61K0047-06 [I,A]; A61K0047-06 [I,C]; A61K0047-10 [I,A]; A61K0047-10 [I,C]; A61K0047-12 [I,A]; A61K0047-12 [I,C]; A61K0047-14 [I,A]; A61K0047-14 [I,C]; A61K0047-30 [I,A]; A61K0047-30 [I,C]; A61K0009-20 [I,A]; A61K0009-20 [I,C]; A61K0009-22 [I,A]; A61K0009-22 [I,C]; A61P0031-00 [I,C]; A61P0031-04 [I,A]; C07H0017-00 [I,C]; C07H0017-08 [I,A]
EPC C07H0017-08F
AB WO 2002038577 A2 UPAB: 20060119
NOVELTY - A pharmaceutical composition comprises an erythromycin derivative and at least one member selected from a long chain

hydrocarbon, a long chain carboxylic acid, a long chain carboxylic ester and a long chain alcohol.

DETAILED DESCRIPTION - A pharmaceutical composition for an extended release of erythromycin derivative in the gastrointestinal environment comprises an erythromycin derivative and at least one member selected from a long chain hydrocarbon, a long chain carboxylic acid, a long chain carboxylic ester and a long chain alcohol. The erythromycin derivative in the composition has an extended release profile.

An INDEPENDENT CLAIM is included for tablet comprising an erythromycin derivative and at least one member selected from long chain hydrocarbon, long chain carboxylic acid and long chain alcohol.

ACTIVITY - Antibacterial.

No suitable biological data given.

MECHANISM OF ACTION - None given in source material.

USE - For an extended release of erythromycin derivative in the gastrointestinal environment, for treating bacterial infection in a host (claimed).

ADVANTAGE - The composition provides sustained release of the erythromycin derivative, can induce a statistically significantly lower mean fluctuation index in the plasma than an immediate release composition while maintaining a similar or increased bio-availability. The composition can be prepared without use of polymer.

TECH ORGANIC CHEMISTRY - Preferred Composition: The composition comprises polymer (less than 3, preferably less than 1)wt.%, and the member (1 - 60)wt.%. The composition comprises the erythromycin derivative (45 - 60)wt.%.

Preferred Components: The member is a long chain carboxylic acid ester, a long chain alcohol or a long chain hydrocarbon.

ABEX ADMINISTRATION - The composition is in oral dosage form. The composition provides a dose of the erythromycin derivative (500 - 1000 mg) and is administered for a period of 5 - 14 days.

SPECIFIC COMPOUNDS - 6-O-Methoxyerythromycin A is specifically claimed as the erythromycin derivative.

EXAMPLE - A tablet composition was prepared as follows: glyceryl monostearate (30 %) was melted and clarithromycin (50 %) was added, cooled and then milled through a screen. The mixture was blended with lactose (19 %) in blender for 20 minutes. Magnesium stearate (1 %) was added and blended for 5 minutes. The blend was compressed using a rotary tablet press

L173 ANSWER 16 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 2002-055556 [07] WPIX Full-text

ED 20050524

DNC C2002-015917 [07]

TI New arzoxifene compositions, useful for treating e.g. CNS disorders, cancers, osteoporosis, hyperlipidemia and cardiovascular diseases,

containing methionine, acetylcysteine or cysteine or their salts as stabilizing agents

DC B02

IN ANN T C; BASHORE F; BASHORE F N; CLARK R E; DEAN M M; HARTAUER K; HARTAUER K J; JOHN H K; MINNETT M; MINNETT M D; NAJJAR B F; RICKARD E; RICKARD E C; TINGLE C; TINGLE C A; BASHORE N; HARTAUER J; MINNETT D; RICKARD C; TINGLE A

PA (BASH-I) BASHORE F N; (HART-I) HARTAUER K J; (ELIL-C) LILLY & CO ELI; (MINN-I) MINNETT M D; (RICK-I) RICKARD E C; (TING-I) TINGLE C A

CYC 96

PI WO 2001085147 A2 20011115 (200207)* EN 67[12]
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AU 2001055310 A 20011120 (200219) EN
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NO 2002005219 A 20021031 (200305) NO
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CZ 2002003651 A3 20030212 (200317) CS
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BR 2001010620 A 20030401 (200327) PT
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SK 2002001565 A3 20030401 (200331) SK
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KR 2003009477 A 20030129 (200336) KO
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US 20030119875 A1 20030626 (200343) EN
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EP 1357903 A2 20031105 (200377) EN
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HU 2003002190 A2 20031028 (200379) HU
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JP 2003535827 W 20031202 (200382) JA 63
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MX 2002010923 A1 20030301 (200413) ES
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ZA 2002007651 A 20040225 (200419) EN 73
NZ 521393 A 20040827 (200460) EN
CN 1545413 A 20041110 (200514) ZH
AU 2001255310 B8 20050303 (200523) EN
AU 2005200809 A1 20050317 (200524)# EN
AU 2001255310 B2 20050303 (200528) EN
TW 225787 B1 20050101 (200620) ZH
MX 235238 B 20060327 (200651) ES
US 7122203 B2 20061017 (200668) EN
AU 2005200809 B2 20060511 (200681)# EN
EP 1357903 B1 20061220 (200702) EN
EP 1757291 A2 20070228 (200718) EN
CN 1283250 C 20061108 (200720) ZH

DE 60125416 E 20070201 (200722) DE
ES 2276784 T3 20070701 (200746) ES
DE 60125416 T2 20070927 (200763) DE
PH 1200101079 B1 20070927 (200854) EN

ADT WO 2001085147 A2 WO 2001-US11736 20010430; US 7122203 B2 Provisional US 2000-203235P 20000508; AU 2001055310 A AU 2001-55310 20010430; AU 2001255310 B8 AU 2001-255310 20010430; AU 2001255310 B2 AU 2001-255310 20010430; AU 2005200809 A1 Div Ex AU 2001-255310 20010430; AU 2005200809 B2 Div Ex AU 2001-255310 20010430; BR 2001010620 A BR 2001-10620 20010430; CN 1545413 A CN 2001-809129 20010430; CN 1283250 C CN 2001-809129 20010430; DE 60125416 E DE 2001-60125416 20010430; DE 60125416 T2 DE 2001-60125416 20010430; EP 1357903 A2 EP 2001-928454 20010430; EP 1357903 B1 EP 2001-928454 20010430; EP 1757291 A2 Div Ex EP 2001-928454 20010430 ; DE 60125416 E EP 2001-928454 20010430; ES 2276784 T3 EP 2001-928454 20010430; DE 60125416 T2 EP 2001-928454 20010430; JP 2003535827 W JP 2001-581801 20010430; NZ 521393 A NZ 2001-521393 20010430; NO 2002005219 A WO 2001-US11736 20010430; CZ 2002003651 A3 WO 2001-US11736 20010430; BR 2001010620 A WO 2001-US11736 20010430; SK 2002001565 A3 WO 2001-US11736 20010430; US 20030119875 A1 WO 2001-US11736 20010430; EP 1357903 A2 WO 2001-US11736 20010430; HU 2003002190 A2 WO 2001-US11736 20010430; JP 2003535827 W WO 2001-US11736 20010430; MX 2002010923 A1 WO 2001-US11736 20010430; NZ 521393 A WO 2001-US11736 20010430; MX 235238 B WO 2001-US11736 20010430; US 7122203 B2 WO 2001-US11736 20010430; EP 1357903 B1 WO 2001-US11736 20010430; DE 60125416 E WO 2001-US11736 20010430; DE 60125416 T2 WO 2001-US11736 20010430; TW 225787 B1 TW 2001-110500 20010502; CZ 2002003651 A3 CZ 2002-3651 20010430; SK 2002001565 A3 SK 2002-1565 20010430; ZA 2002007651 A ZA 2002-7651 20020923; US 20030119875 A1 US 2002-258273 20021018; US 7122203 B2 US 2002-258273 20021018; NO 2002005219 A NO 2002-5219 20021031; MX 2002010923 A1 MX 2002-10923 20021106; MX 235238 B MX 2002-10923 20021106; KR 2003009477 A KR 2002-714323 20021107; HU 2003002190 A2 HU 2003-2190 20010430; AU 2005200809 A1 AU 2005-200809 20050223; AU 2005200809 B2 AU 2005-200809 20050223; EP 1757291 A2 EP 2006-122957 20010430; EP 1357903 B1 Related to EP 2006-122957 20061025; PH 1200101079 B1 PH 2001-1079 20010504

FDT AU 2001255310 B8 Previous Publ AU 2001255310 A; AU 2001255310 B2 Previous Publ AU 2001255310 A; EP 1757291 A2 Div ex EP 1357903 A; DE 60125416 E Based on EP 1357903 A; ES 2276784 T3 Based on EP 1357903 A; AU 2001055310 A Based

on WO 2001085147 A; CZ 2002003651 A3 Based on WO 2001085147 A; BR 2001010620 A Based on WO 2001085147 A; SK 2002001565 A3 Based on WO 2001085147 A; EP 1357903 A2 Based on WO 2001085147 A; HU 2003002190 A2 Based on WO 2001085147 A; JP 2003535827 W Based on WO 2001085147 A; MX 2002010923 A1 Based on WO 2001085147 A; NZ 521393 A Based on WO 2001085147 A; AU 2001255310 B8 Based on WO 2001085147 A; AU 2001255310 B2 Based on WO 2001085147 A; MX 235238 B Based on WO 2001085147 A; US 7122203 B2 Based on WO 2001085147 A; EP 1357903 B1 Based on WO 2001085147 A; DE 60125416 E Based on WO 2001085147 A; DE 60125416 T2 Based on EP 1357903 A; DE 60125416 T2 Based on WO 2001085147 A

PRAI US 2000-203235P 20000508
US 2002-258273 20021018
AU 2005-200809 20050223

IC ICM A61K; A61K031-00; A61K031-445; A61K031-4535; A61K047-18
ICS A61K047-20; A61K009-20; A61K009-48; A61P013-08; A61P015-00; A61P019-08; A61P019-10; A61P025-00; A61P025-28; A61P003-06; A61P035-00; A61P043-00; A61P009-08; A61P009-10; C07D333-64; C07D409-12; C07D413-12

IPCI A61K0031-00 [I,A]; A61K0031-00 [I,A]; A61K0031-00 [I,C]; A61K0031-00 [I,C]; A61K0031-445 [I,A]; A61K0031-445 [I,A]; A61K0031-445 [I,A]; A61K0031-445 [I,C]; A61K0031-445 [I,C]; A61K0031-445 [I,C]; A61K0031-445 [I,C]; A61K0047-16 [I,C]; A61K0047-16 [I,C]; A61K0047-16 [I,C]; A61K0047-18 [I,A]; A61K0047-18 [I,A]; A61K0009-20 [I,A]; A61K0009-20 [I,A]; A61K0009-20 [I,A]; A61K0009-20 [I,C]; A61K0009-20 [I,C]; A61K0009-20 [I,C]; A61K0009-20 [I,C]; A61K0009-20 [I,C]; A61P0035-00 [I,A]; A61P0035-00 [I,C]

IPCR A61K0031-00 [I,A]; A61K0031-00 [I,C]; A61K0031-4523 [I,C]; A61K0031-4535 [I,A]; A61K0047-16 [I,C]; A61K0047-18 [I,A]; A61K0047-20 [I,A]; A61K0047-20 [I,C]; A61K0009-20 [I,A]; A61K0009-20 [I,C]; A61K0009-48 [I,A]; A61K0009-48 [I,C]; A61P0013-00 [I,C]; A61P0013-08 [I,A]; A61P0015-00 [I,A]; A61P0015-00 [I,C]; A61P0019-00 [I,C]; A61P0019-08 [I,A]; A61P0019-10 [I,A]; A61P0025-00 [I,A]; A61P0025-00 [I,C]; A61P0025-28 [I,A]; A61P0003-00 [I,C]; A61P0003-06 [I,A]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0043-00 [I,A]; A61P0043-00 [I,C]; A61P0009-00 [I,C]; A61P0009-08 [I,A]; A61P0009-10 [I,A]

EPC A61K0031-4535; A61K0047-18B; A61K0009-20H4

NCL NCLM 514/324.000

AB WO 2001085147 A2 UPAB: 20060118
NOVELTY - A novel pharmaceutical formulation (I) comprises:
(1) 6-hydroxy-3-(4-(2-(piperidin-1-yl)ethoxy)phenoxy)-2-(4-methoxyphenyl)benzo(b)thiophene or arzoxifene (Ia) or its salt; and
(2) a stabilizing agent, selected from methionine, acetylcysteine or cysteine or their salts, in an amount sufficient to effect stabilization against decomposition.

DETAILED DESCRIPTION - A novel pharmaceutical formulation (I) comprises:

(1) 6-hydroxy-3-(4-(2-(piperidin-1-yl)ethoxy)phenoxy)-2-(4-methoxyphenyl)benzo(b)thiophene or arzoxifene of formula (Ia) or its salt; and

(2) a stabilizing agent, selected from methionine, acetylcysteine or cysteine or their salts, in an amount sufficient to effect stabilization against decomposition.

INDEPENDENT CLAIMS are also included for:

(1) use of a formulation (I) in the manufacture of a medicament for the treatment of uterine fibrosis, endometriosis, aortal smooth muscle cell proliferation, restenosis, breast cancer, uterine cancer, prostatic cancer or benign prostatic hyperplasia, bone loss, osteoporosis, cardiovascular disease, hyperlipidemia, CNS disorders or Alzheimer's disease;

(2) a method of stabilizing a pharmaceutical formulation comprising (Ia) against decomposition comprising incorporation of a stabilizing agent selected from methionine, acetylcysteine or cysteine or their salts in addition to 6-hydroxy-3-(4-(2-(piperidin-1-yl)ethoxy)phenoxy)-2-(4- methoxyphenyl)benzo(b)thiophene or its salt.

ACTIVITY - Cytostatic; Gynecological; Cardiant; Vasotropic; Osteopathic; Antilipemic; Neuropathic; Neuroprotective; Nootropic.

MECHANISM OF ACTION - The arzoxifene is a nonsteroidal mixed estrogen antagonist/agonist.

USE - The compositions (F-I), (F-III) and (F-V) may be used in the manufacture of a medicament to inhibit uterine fibrosis, endometriosis, aortal smooth muscle cell proliferation, restenosis, breast cancer, uterine cancer, endometrial cancer prostatic cancer, or benign prostatic hyperplasia, bone loss, osteoporosis, cardiovascular disease, hyperlipidemia, CNS disorders or Alzheimer's disease (claimed).

ADVANTAGE - The stabilizing agents greatly reduce the formation of degradation products during the manufacturing process and/or storage of the drug product. The F-I, F-III and F-V forms of (Ia) hydrochloride are more stable at ambient temperature and therefore more amenable to pharmaceutical development as compared to crystal forms in US5723474. F-I and F-III are much more crystalline than the form disclosed in US5723474. Unlike the form of arzoxifene hydrochloride produced by the procedures in US5723474, which contained ethyl acetate and water in its lattice, F-I and F-III contain only water. Unlike S-II, F-I and F-III, F-V is truly an anhydrous form of arzoxifene hydrochloride which shows so propensity to adsorb water on changes in relative humidity. F-V's crystal lattice is stable up to its melting temperature. F-V has approximately10% higher aqueous solubility relative to F-III and is

the thermodynamically most stable known form of arzoxifene hydrochloride at ambient storage conditions.

Core tablets weighing approximately 250 mg and containing approximately 10 mg or 20 mg of arzoxifene as arzoxifene hydrochloride were prepared and then assayed for their levels of degradation products (N-oxide, cleavage product and total). Analysis for the arzoxifene N-oxide degradation product, the arzoxifene cleavage product and total related substances (process related impurities plus degradation products) was performed using a gradient HPLC method. The results showed that the presence of cysteine hydrochloride at 0.5 mg/tablet in both strengths of arzoxifene tablets, resulted in an order of magnitude reduction in the N-oxide level after 6 months storage at 40 degrees C relative to the formulation with no stabilizer. Increases in the level of the cleavage product were also significantly reduced by approximately a factor of two in the presence of cysteine hydrochloride compared to those lots which did not contain the stabilizer.

TECH PHARMACEUTICALS - Preferred formulation: (Ia) is preferably present as the hydrochloride salt, e.g. the crystalline hydrochloride hydrate. The stabilizing agent may be present in the formulation at 0.01-10 wt.%, preferably 0.05-5.0 wt.% of the total formulation. The stabilizing agent may be e.g. cysteine hydrochloride, L-cysteine hydrochloride monohydrate. The compositions may contain 20-23 mg, preferably 21.53 mg of (Ia) hydrochloride, and 0.2-0.8 mg, preferably 0.5 mg of cysteine hydrochloride, or 5.3-5.9 mg, preferably 5.62 mg of (Ia) hydrochloride, and 0.2-0.3 mg, preferably 0.25 mg of cysteine hydrochloride.

ORGANIC CHEMISTRY - Preferred formulation: The formulations (I) comprise 6-hydroxy-3-(4-(2-(piperidin-1-yl)ethoxy)phenoxy)-2-(4-methoxyphenyl)benzo(b)thiophene hydrochloride in the form of crystalline (Ia) hydrochloride hydrate:

(i) (F-I) having an X-ray diffraction d line spacing pattern comprising the following peaks: 7.91 +/-0.2, 10.74 +/-0.2, 14.86 +/-0.2, 15.92 +/-0.2, 18.28 +/-0.2, and 20.58 +/-0.2 degrees in 2-theta, when obtained from a copper radiation source;

(ii) (F-III) having an X-ray diffraction d line spacing pattern comprising the following peaks: 4.63 +/-0.2, 7.82 +/-0.2, 9.29 +/-0.2, 13.97 +/-0.2, 17.62 +/-0.2, 20.80 +/-0.2, and 24.31 +/-0.2 degrees in 2- theta, when obtained at 25 +/-2 degrees C and 35 +/-10% relative humidity from a copper radiation source;

or

(iii) (F-V) having an X-ray diffraction pattern comprising at least one of the following peaks: 7.3 +/-0.2, 15.5 +/-0.2, 15.9 +/-0.2, and 17.6 +/-0.2 degrees in 2-theta when obtained from a copper radiation source.

The X-ray diffraction pattern of (F-V) further comprises the

following peaks: 17.9 +/-0.2, 18.2 +/-0.2, 18.9 +/-0.2, 21.5 +/-0.2 degrees in 2-theta when obtained from a copper radiation source. Preparation: The arzoxifene may be obtained as in US5723474 and US5510357. The crystallization procedure was modified so that ethanol was added to a suspension of crude arzoxifene hydrochloride in refluxing ethyl acetate. Upon cooling and vacuum filtration, the solid that resulted was a highly crystalline mixed ethyl acetate/water solvate of arzoxifene hydrochloride (S-II). F-I (another crystalline form of arzoxifene hydrochloride) was prepared by removing the ethyl acetate from S-II's crystal lattice by vacuum drying/annealing S-II at elevated temperatures. F-III was readily prepared and isolated at ambient temperature by crystallization of arzoxifene hydrochloride (or any polymorph/solvate) from a mixture of isopropyl alcohol (IPA) and water. F-V may be prepared by drying, either at ambient temperature or at slightly elevated temperature, the crystalline solid isolated at ambient temperature from crystallization of arzoxifene hydrochloride (or any polymorph/solvate from methanol, ethanol, or isopropanol or aqueous mixtures of methanol.

ABEX ADMINISTRATION - The compositions may be administered in a tablet or capsule form (claimed). (Ia) may be used in doses of e.g. 0.1-100, preferably 1-40 mg/day. EXAMPLE - Core tablets weighing approximately 250 mg and containing approximately 10 mg or 20 mg of arzoxifene as arzoxifene hydrochloride were prepared generally as follows: the arzoxifene hydrochloride, water soluble diluents (lactose monohydrate and anhydrous lactose), and a portion of the disintegrant (crospovidone) were blended in a high shear granulator. This blend was then wet massed in the high shear granulator with an aqueous solution of povidone and polysorbate 80. In those formulations which contain the stabilizer (cysteine hydrochloride), the cysteine hydrochloride was also dissolved in the granulation solution and added during the wet mass step via the granulation solution. Following a wet sizing step though a rotating impeller mill, the granules were dried using a fluid bed dryer. The dried granules were reduced to a suitable size with a rotating impeller mill. The remaining ingredients (microcrystalline cellulose, magnesium stearate, and the rest of the crospovidone) were added to the dried granules and blended. This mixture was then compressed into round shaped tablets using a conventional rotary tablet press

L173 ANSWER 17 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2001-367355 [38] WPIX Full-text
ED 20050525
DNC C2001-112614 [38]
TI Drug delivery device comprising a core comprising a beneficial agent

and optionally a pH modulating agent and a controlled porosity, microporous coating

DC B03; B07; P32; P34

IN DEBUSI L A; RUDDY S B; STOREY D E

PA (MERI-C) MERCK & CO INC

CYC 92

PI WO 2001032149 A1 20010510 (200138)* EN 57[4]
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AU 2001014443 A 20010514 (200149) EN
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EP 1227800 A1 20020807 (200259) EN
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JP 2003513033 W 20030408 (200333) JA 61
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ADT WO 2001032149 A1 WO 2000-US29868 20001027; EP 1227800 A1 EP 2000-976707 20001027; EP 1227800 A1 WO 2000-US29868 20001027; JP 2003513033 W WO 2000-US29868 20001027; AU 2001014443 A AU 2001-14443 20001027; JP 2003513033 W JP 2001-534354 20001027

FDT AU 2001014443 A Based on WO 2001032149 A; EP 1227800 A1 Based on WO 2001032149 A; JP 2003513033 W Based on WO 2001032149 A

PRAI US 1999-162719P 19991029
US 1999-162589P 19991029

IC ICM A61K009-00

IPCR A61D0007-00 [I,A]; A61D0007-00 [I,C]; A61K0031-00 [I,A]; A61K0031-00 [I,C]; A61K0031-337 [I,A]; A61K0031-337 [I,C]; A61K0031-496 [I,A]; A61K0031-496 [I,C]; A61K0045-00 [I,A]; A61K0045-00 [I,C]; A61K0047-12 [I,A]; A61K0047-12 [I,C]; A61K0009-00 [I,A]; A61K0009-00 [I,C]; A61K0009-22 [I,A]; A61K0009-22 [I,C]; A61K0009-30 [I,C]; A61K0009-32 [I,A]; A61K0009-36 [I,A]; A61N0005-10 [I,A]; A61N0005-10 [I,C]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0043-00 [I,A]; A61P0043-00 [I,C]

EPC A61K0009-00L4; A61K0031-00+A; A61K0031-496

AB WO 2001032149 A1 UPAB: 20050525

NOVELTY - Drug delivery device comprising a core comprises a beneficial agent and optionally a pH modulating agent and a controlled porosity, microporous coating optionally with an aperture.

DETAILED DESCRIPTION - A pH insensitive drug delivery device for the controlled release of a beneficial agent in an environment of use, comprises: (a) a core prepared from an admixture comprising at least one beneficial agent or salt, that has a solubility profile that is dependent on the pH level of the environment of use, and at least one pH modulating agent; and (b) a controlled porosity, microporous coating which surrounds the core.

An INDEPENDENT CLAIM is also included for an osmotic drug delivery device for the controlled release of a beneficial agent in an environment of use, comprising: (a) a core containing at least one

beneficial agent or salt, that has a solubility profile that is dependent on the pH level of the environment of use; and (b) a controlled porosity, microporous coating which surrounds the core and has at least one aperture.

USE - The devices can be used for the delivery of agents such as a prenyl protein transferase inhibitor, e.g. 1-(3-chlorophenyl)-4-(1-(4-cyanobenzyl)-5-imidazolyl methyl)-2-piperazinone for the treatment of cancer or for conferring radiation sensitivity to a tumor cell (claimed). Such devices can be used in combination with an antineoplastic agent, e.g. paclitaxel (claimed).

ADVANTAGE - The devices can provide for the controlled release of a beneficial agent across a range of physiologically relevant pH levels for up to a 24 hour period. The addition of a pH modulating agent to the drug delivery device provides an improved, controlled-release that is generally insensitive to the pH level of the environment of use.

TECH PHARMACEUTICALS - Preferred Drugs: The beneficial agent may be a prenyl protein transferase inhibitor especially 1-(3-chlorophenyl)-4-(1-(4-cyanobenzyl)-5-imidazolyl methyl)-2-piperazinone. The amount of beneficial agent may be 0.1-95 wt.%, preferably 10-20 wt.% of the total core mixture. The microporous coating may have apertures exposing 0.05-0.5% of the core surface. The aperture may be circular with a diameter of 0.1-0.5 mm.

ORGANIC CHEMISTRY - The pH modulating agent may be an organic acid, e.g. succinic acid, citric acid or tartaric acid.

ABEX EXAMPLE - A formulation was prepared using 1-(3-chlorophenyl)-4-(1-(4-cyanobenzyl)-5-imidazolyl methyl)-2-piperazinone HCl (compound A) as the beneficial agent. Tablets were prepared with a core using 109.0 mg compound A, 81.0 mg succinic acid, 2.0 mg magnesium stearate, NF (non-bovine), 10.0 g polyvinyl pyrrolidone (K-29/32) and 50 mg 2-propanol to a total tablet weight of 202 mg. Compound A, succinic acid and polyvinyl pyrrolidone were dry mixed in a mixer and wet granulated using 100% isopropanol. The resulting granules were dried and milled, and subsequently lubricated with magnesium stearate. The lubricated granules were compressed at a target weight of 202 mg and were compressed on a small rotary tablet press. In certain cases, the tablet cores were film-coated using an aqueous solution of hydroxypropyl cellulose (HPC) and hydroxypropyl methylcellulose (HPMC) in a side-vented pan coater. The tablets were then charged to a fluid bed column coater using a solution of cellulose acetate, sucrose and polyethylene glycol 400, in a trisolvent vehicle comprising acetone, methanol and water. The thickness of the resulting controlled porosity, microporous coating ranged from 150 to 200 microm. The tablets provide pH-insensitive controlled release of compound A.

L173 ANSWER 18 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2001-273084 [28] WPIX Full-text
ED 20050525
DNC C2001-082741 [28]
TI Recovery of juice from Echinacea plant material, useful for producing an immunostimulant powder, comprises blanching the material before squeezing it to express the juice
DC B04
IN BROVELLI E; LI Y; MENON G R; RANA J
PA (AMWA-N) AMWAY CORP
CYC 1
PI US 6217878 B1 20010417 (200128)* EN 6[1]
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ADT US 6217878 B1 US 1999-373943 19990813
PRAI US 1999-373943 19990813
IPCR A61K0036-185 [I,C]; A61K0036-28 [I,A]
EPC A23L0001-30B; A23L0002-04; A61K0036-28
NCL NCLM 424/737.000
AB US 6217878 B1 UPAB: 20050525
NOVELTY - A process (A) for recovering juice from Echinacea plant material (I), comprising blanching (I) before squeezing it to express the juice, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a process (B) for producing a powder containing water-soluble solids of (I), comprising:

(a) milling (I);

(b) blanching the milled material with steam;

(c) expressing juice from the blanched material;

(d) concentrating the juice to produce a concentrate having a soluble solids content of at least 20 %; and

(e) drying the concentrate to produce a powder with a moisture content below 8 %.

ACTIVITY - Immunostimulant.

No biological data is given.

MECHANISM OF ACTION - None given.

USE - The juice is useful for making a powder comprising water-soluble solids of (I), which are useful as an immunostimulant for enhancing the body's immune response, e.g. in tablet form or as a component of a blended supplement.

ADVANTAGE - Blanching inactivates enzymes that degrade cichoric acid and softens (I) to increase the yield of juice, preferably by 17 %.

TECH PHARMACEUTICALS - Preferred Process (A): In the process of (A), (I) is milled to a particle size of less than 2 inches before blanching. Blanching is effected by heating (I) to at least 180 degrees F for at least 1 minute, especially by steaming for at least 2 minutes. In the process of (B) juice is expressed by

pressing the blanched material to produce juice in an amount of at least 40 %, by weight, of the blanched material. The juice is aged for at least 6 hours before being concentrated by vacuum evaporation. A carrier is added to the concentrate, preferably in an amount of 25-100 % of the soluble solids content of the juice, to reduce loss of soluble solids during drying. The concentrate is pasteurized before being spray dried at an inlet temperature of 300-330 degrees F and an outlet temperature of 200-220 degrees F. The resulting powder has a cichoric acid content of at least 1.5, preferably at least 3.5 %.

ABEX EXAMPLE - Aerial parts of Echinacea purpurea plants were chopped using an Urschel chopper with a 0.24 inch mill head. The milled material (100.65 kg) was blanched with steam at 100 degrees C for 2 minutes. The blanched material (113.91 kg) was pressed in a hydraulic press and the juice (56.6 kg) was concentrated by vacuum evaporation to obtain a concentrate (14.8 kg) with a soluble solids content of 30.8 %. This was combined with maltodextrin (25 % of solids), pasteurized at 180 degrees F for 3 minutes, and spray dried at an inlet temperature of 310 degrees F and an outlet temperature of 200 degrees F. The resulting powder had a cichoric acid content of 3.67 %.

IT UPIT 20050525
208229-CL 208229-PRD

FS CPI

MC CPI: B04-A08C2; B04-A09; B04-A10; B14-G01

CMC UPB 20050525
M1 *01* M423 M720 N104 N161 P434 M905
DCN: RA060S-K RA060S-P RA060S-T
DCR: 208229-K 208229-P 208229-T
M6 *02* P434 R502 R521 R527 R535 M905

L173 ANSWER 19 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 2001-244367 [25] WPIX

ED 20050705

DNC C2001-073308 [25]

TI New compositions containing drospirenone and ethinylestradiol, useful for inhibiting ovulation in mammals and for treating androgen-induced disorders

DC B01

IN HEIL W; HEITHECKER R; HILMAN J; HILMANN J; HUEMPEL M; LIPP R; TACK J W

PA (SCHD-C) SCHERING AG; (HEIL-I) HEIL W; (HEIT-I) HEITHECKER R; (HILM-I) HILMAN J; (LIPP-I) LIPP R; (FARB-C) BAYER SCHERING PHARMA AG

CYC 94

AB WO 2001015701 A1 UPAB: 20060202

NOVELTY - Compositions containing 2-4 mg (daily dosage) 15beta, 16beta-dimethylene-3-oxo-17alpha-pregn-4-ene-21, 17-carbolactone (drospirenone, I) and 0.01-0.05 mg (daily dosage) 17alpha-ethinylestradiol (ethinylestradiol; II) and carriers or excipients, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a pharmaceutical preparation consisting of a number of separately packaged and individually removable daily dosage units placed in a packaging unit and intended for oral administration for at least 21 consecutive days, where the daily dosage units comprises a combination of drospirenone (2-4 mg) and ethinylestradiol (0.01-0.05 mg);

(2) a pharmaceutical preparation consisting of a number of separately packaged and individually removable daily dosage units placed in a packaging unit and intended for oral administration for 28 consecutive days, where at least 21 of the daily dosage units comprises a combination of drospirenone in an amount of 2 to 4 mg and ethinylestradiol in an amount of 0.01 to 0.05 mg, and where 7 or less of the daily dosage units contain ethinylestradiol alone in an amount of 0.01 to 0.05 mg;

(3) a method of promoting rapid dissolution of drospirenone from a unit dosage form on oral administration comprising providing drospirenone in micronized form in the unit dosage form, or sprayed from a solution onto particles of an inert carrier in admixture with one or more excipients that promote dissolution of the drospirenone.

ACTIVITY - Contraceptive; gynecological; antiseborrheic; antiacne; dermatological.

An open-label, randomized trial with 52 female volunteers aged 20-35 years included 1 pre-treatment cycle, 3 treatment cycles with 2 different tablets containing 2 mg and 3 mg drospirenone, respectively, and a follow-up phase. A wash-out phase of 1 month preceded the treatment. At defined time points, selected central and peripheral parameters were investigated: LH, FSH, 17beta-estradiol, progesterone, cervical score, spinnbarkeit, fern phenomenon. Ovarian function was checked by ultrasound. In addition, SHBG, CBG, prolactine, total testosterone, androstenedione, DHEA-S and selected metabolic parameters (serum glucose, triglycerides, cholesterol, HDL, LDL) were examined. Blood pressure, heart rate, body weight and cycle control were documented. The results of the study showed that both LH and FSH were clearly suppressed with both trial preparations. Accordingly, the secretion of estradiol and progesterone were greatly reduced over all 3 treatment cycles with the exception of 3 volunteers receiving the 2 mg drospirenone preparation. Follicular ripening occurred in several cases with both trial preparations. No differences were demonstrable statistically (pat least0.05) between the 2 trial preparations as regards the hormones LH, FSH, estradiol

and progesterone, and the parameter ovulation during the treatment cycles. In keeping with the hormones, cervical function was greatly limited and the spinnbarkeit and crystallizability of the cervical mucus was greatly reduced with both trial preparations. Triglycerides and HDL levels increased with both trial preparations, while LDL levels decreased. Total cholesterol was largely unchanged in both treatment groups. Oral glucose tolerance remained virtually unchanged or was slightly decreased. Testosterone, androstenedione and DHEA-S decreased minimally. The results confirmed the results of earlier studies that the 2 mg drospirenone preparation was in the threshold region of ovulation, whereas the 3 mg drospirenone preparation had a demonstrable ovulation-inhibiting effect in all cases examined.

MECHANISM OF ACTION - Ovulation inhibitor.

USE - The compositions can be used for inhibiting ovulation in mammals, particularly humans (claimed). They can also be used for preventing or treating androgen-induced disorders in a female mammal, e.g. acne (claimed). Since drospirenone is an aldosterone antagonist, it has diuretic properties and is therefore suitable for counteracting the water-retentive properties of ethinylestradiol.

ADVANTAGE - The compositions can reduce the minimum dosage level of drospirenone required for reliable contraceptive activity. They can provide for rapid absorption of drospirenone in vivo on oral administration of the compound. This is an advantage because isomerization of the compound in the gastric environment and/or hydrolysis in the intestine is substantially reduced, leading to a high bioavailability of the compound.

TECH PHARMACEUTICALS - Preferred Composition: At least 70%, preferably 80% (I) and (II) are released within 30, preferably 20 minutes of administration. (I) and (II) may be applied in micronized form or sprayed from a solution onto particles of an inert carrier. Composition comprises 2-4, preferably 3-3.5 mg/daily dose (I) and 0.01-0.05, preferably 0.03-0.04 mg/daily dose (II). Number of daily dosage units of (I) and (II) is 21-4, and the number of daily dosage units with no active agent is 4-7. Number of daily dosages of the composition are 28, 56 or 84.

ABEX ADMINISTRATION - The compositions are preferably administered orally with 2-4, preferably 3-3.5 mg/day of drospirenone and 0.01-0.05, preferably 0.03-0.04 mg ethinylestradiol.

EXAMPLE - Tablet cores of the following composition: 3.00 mg micronized drospirenone, 0.03 mg micronized ethinylestradiol, 48.17 mg lactose monohydrate, 14.40 mg corn starch, 9.60 mg modified starch, 4.00 mg polyvinylpyrrolidone 25000, and 0.80 mg magnesium stearate, were prepared by charging a fluidized bed granulator with 31.68 kg corn starch, 21.12 kg modified starch, 6.60 micronized drospirenone, 0.066 kg micronized ethinylestradiol and 105.974 kg lactose monohydrate and activating the fluidized bed. An aqueous solution of 8.80 kg polyvinylpyrrolidone 2500 in 46.20 mg purified

water was sprayed continuously onto the fluidized bed while drying by heating the air stream of the fluidized bed.
At the end of the process 1.76 kg magnesium stearate was sucked into the granulator and mixed with the granules by maintaining the fluidized bed. The resulting granulate was pressed into tablet cores by compression using a rotary tablet press. 2.22464 kg of hydroxypropylmethylcellulose and 0.44528 kg macrogol 6000 were dissolved in 14.67 kg purified water. 0.44528 kg talc, 1.22430 kg titanium dioxide and 0.06050 kg ferric oxide pigment were suspended in 10.26 kg purified water with stirring and homogenized. The solution and suspension were combined and used to coat the table cores by continuous application of the coating suspension in a coater.

IT UPIT 20060202
93722-CL 93722-USE; 94585-CL
FS CPI
MC CPI: B01-A02; B01-C05; B14-D02A; B14-N17D; B14-P01B
CMC UPB 20060202
DRN: 0141-U
DCR: 94585-U
M5 *01* M431 M781 M782 P611 P842 P943 M905 M904
RIN: 45911 49740
DCN: RA02G5-K RA02G5-M RA02G5-T RA02G5-U
DCR: 93722-K 93722-M 93722-T 93722-U
M5 *02* M431 M782 P611 P842 P943 M905 M904 M910
DCN: R00141-K R00141-M R00141-T
DCR: 94585-K 94585-M 94585-T 94585-U

L173 ANSWER 20 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2001-205074 [21] WPIX Full-text
ED 20050525
DNC C2001-061205 [21]
DNN N2001-146570 [21]
TI Lozenges useful for treating inflammation in throat, bronchus and oral cavity, comprises reduced palatinose as base material to form crystal layer on surface
DC B07; P33
IN NAKAI Y
PA (TAKA-N) TAKAICHI SEIYAKU KK
CYC 1
PI JP 2000327563 A 20001128 (200121)* JA 4[0]
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ADT JP 2000327563 A JP 1999-135683 19990517
PRAI JP 1999-135683 19990517
IPCR A61J0003-06 [I,A]; A61J0003-06 [I,C]; A61K0047-26 [I,A]; A61K0047-26 [I,C]; A61K0009-30 [I,C]; A61K0009-36 [I,A]

AB JP 2000327563 A UPAB: 20050525

NOVELTY - Lozenges comprising medicinal components, is shaped into granules. Reduced palatinose as base material is added to form a crystal layer on the surface.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the manufacture of lozenges which involves mixing reduced palatinose as base and a medicinal component. The mixture is granulated and compressed into solid. A crystal layer of reduced palatinose having moisture content adjusted to 0.7-1.58 %, is formed on the surface by pressing the granules at 50-70 % humidity is covered by crystal layer at 15-35 degrees C for 5-24 hours. A hard crystal layer of reduced palatinose is formed.

USE - As lozenges for use in medical treatments such as inflammation of throat, bronchus and oral cavity.

ADVANTAGE - The granular shape of the lozenges is maintained by the strength of the crystal layer, high physical property and the low hydroscopic property of reduced palatinose. The moisture content of the pre-formulation is adjusted and thereby the moldability is favored. The crystal growth in the layer is controlled by adjusting moisture content, thereby the cloudiness on the lozenges is prevented. The storage stability, efficacy of the drug, shape and color tone of the lozenges is increased. Since the lozenges contains homogeneous composition, both inside and as a coating, there is no taste difference and odd feeling in the mouth. The lozenges can be manufactured efficiently by forming crystal layer of suitable thickness.

ABEX EXAMPLE - Palatinose was added to water and reduced by heating. The reduced palatinose was added with potassium guaiacol sulfonate (0.034 weight %), dextromethorphal phenol phosphates (0.75 weight %) and cetyl chloride pyridinium (0.34 weight %), at 150-160 degrees C and degree of vacuum of 500-600 mmHg. The mixture was shaped to disk-shaped lozenges and granular molding was carried out for 10 hours. The humidity was set to 52 % at 25-28 degrees C and lozenges having crystal layer of reduced palatinose with a thickness of 15 microm was manufactured (A) with moisture content of crystal layer of 1-1.3 weight %. The mixture . A lozenge was prepared by using starch syrup as base material (B) and compared with the above lozenges. Lozenges A and B were exposed to air for 1 month and given to 10 persons. A provided antitussive effect by dissolving and had reduced cloudiness. The flavor of B differed in coating and inside, while dissolving in mouth.

L173 ANSWER 21 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2000-558362 [51] WPIX Full-text
ED 20050412
DNC C2000-166322 [51]

TI Rapidly soluble compositions for e.g. mucosal or oral drug delivery, comprising shaped body formed from open matrix carbohydrate polymer

DC A11; A96; A97; B07; C07

IN COLACO C; MARTYN G P

PA (QUAD-N) QUADRANT HEALTHCARE UK LTD; (QUAD-N) QUADRANT HOLDINGS CAMBRIDGE LTD

CYC 89

PI WO 2000050013 A1 20000831 (200051)* EN 16[0]
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AU 2000026815 A 20000914 (200063) EN
<--
EP 1156785 A1 20011128 (200201) EN
<--
JP 2002537322 W 20021105 (200304) JA 17
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ADT WO 2000050013 A1 WO 2000-GB630 20000222; AU 2000026815 A AU 2000-26815 20000222; EP 1156785 A1 EP 2000-905188 20000222; JP 2002537322 W JP 2000-600625 20000222; EP 1156785 A1 WO 2000-GB630 20000222; JP 2002537322 W WO 2000-GB630 20000222

FDT AU 2000026815 A Based on WO 2000050013 A; EP 1156785 A1 Based on WO 2000050013 A; JP 2002537322 W Based on WO 2000050013 A

PRAI GB 1999-4049 19990222

IPCR A61K0009-20 [I,A]; A61K0009-20 [I,C]

EPC A61K0009-20H6F; A61K0009-20H6F4; A61K0009-20P

ICO K61K0009:20H4B

AB WO 2000050013 A1 UPAB: 20050412
NOVELTY - A vehicle for mucosal or oral delivery of bioactive substances comprises a shaped body composition comprising a rapidly soluble, open matrix of a carbohydrate polymer.
USE - For mucosal or oral delivery of bioactive substances, especially those needing rapid release; also in diagnostic, environmental, agricultural and industrial applications.
ADVANTAGE - The composition avoids the use of gelatin, so can be used by vegetarians, and dissolves more rapidly than other gelatin replacements.

TECH POLYMERS - Preferred Composition: The carbohydrate polymer is hydroxyethyl starch or pullulan. The composition comprises at least one excipient, low molecular weight carbohydrate, coloring and flavoring agents and a therapeutic agent. The vehicle is in the shape of a tablet. Preparation : Solvent is removed (preferably by freeze-drying) from a solution containing the carbohydrate polymer and any other components, the solution being provided as a single dosage aliquot in a mould corresponding to the desired shape.

ABEX EXAMPLE - Solutions of pullulan or hydroxyethyl starch (0.25, 0.5,

1 or 2.5%) in water containing 5% mannitol, raffinose or trehalose, were dispensed in 1 ml aliquots into the wells of a plastic blister pack. The blisters were freeze-dried at -32degreesC, and then a vacuum was turned on and the frozen solutions were lyophilized for 24 hours whilst the temperature rose from -20 to 30degreesC, giving a solid matrix of carbohydrate polymer plus sugar excipient. The matrices were intact, and dissolved instantaneously in water at room temperature, even after a week's storage at ambient temperature and humidity. Only the matrices containing 1 or 2.5% carbohydrate polymer were of sufficiently low friability to be removed as an intact single dosage unit from the blister pack.

L173 ANSWER 22 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2000-412127 [35] WPIX
ED 20050705
DNC C2000-124911 [35]
TI Combined carvedilol and hydrochlorothiazide compositions for the treatment of cardiac and circulatory disorders, e.g. hypertension, angina pectoris and cardiac insufficiency
DC A96; B02
IN HELLER R
PA (HELL-I) HELLER R; (HOFF-C) HOFFMANN LA ROCHE & CO AG F; (HOFF-C) HOFFMANN LA ROCHE INC
CYC 89
AB WO 2000032174 A2 UPAB: 20060116
NOVELTY - Pharmaceutical compositions (I) comprising (as active substances) both carvedilol (or a salt) (Ia) and hydrochlorothiazide (or salt) (Ib), are new.

DETAILED DESCRIPTION - Carvedilol and hydrochlorothiazide have previously been used to treat (for example) hypertension, however, a fixed combination of the 2 agents was not previously available. Carvedilol and hydrochlorothiazide have been marketed as, for example, Dilatrend (RTM) and Esidrex (RTM) (respectively).

INDEPENDENT CLAIMS are also included for the following:

(1) a method (II) for the treatment of cardiac and circulatory disorders such as hypertension, angina pectoris, cardiac insufficiency and/or other associated disorders, comprising the administration of (I);

(2) a process (III) for the production of (I), comprising:

(a) processing a (Ia) granulate and a (Ib) granulate to a pressed mass (the 2 granulates each have a moisture content (MC) of 6-20% and a bulk density (BD) of 0.1-1.5 g/ml (the MC and BD of (Ia) and (Ib) do not vary from one another by more than 30%)); and

(b) the production of a solid dosage form from the pressed mass of step (a); and

(3) a light-protecting film suspension (III) comprising:

(a) 10-15% by weight (wt%) poly(ethyl acrylate) and poly(methylacrylate) in a ratio of 2:1;
(b) 1-10 wt% sodium citrate;
(c) 1-25 wt% methylhydroxypropylcellulose;
(d) 0-20 wt% macrogol;
(e) 5-40 wt% talc;
(f) 2-25 wt% titanium dioxide;
(g) 0-10 wt% indigocarmine color laquer;
(h) 0-2 wt% polysorbate; and/or
(i) 0-1.0 wt% dimethicone.

ACTIVITY - Hypotensive; antianginal; cardioactive.

No biological data given.

MECHANISM OF ACTION - Carvedilol is an alpha-1 blocker and hydrochlorothiazide is a diuretic.

USE - (I) is used for the treatment of cardiac and circulatory disorders such as hypertension, angina pectoris, cardiac insufficiency and/or other associated disorders (claimed).

ADVANTAGE - The carvedilol and hydrochlorothiazide are administered together as a single dosage.

TECH PHARMACEUTICALS - Preferred Compositions: The ratio of (Ia) to (Ib) is 0.5:1 to 10:1. (I) may comprise binders, disintegrants, glidants, adsorption agents, separating agents, fillers and/or carriers as additives. Preferably, (I) comprises:

(i) 0-50% by weight (wt%) lactose;
(ii) 0-50 wt% saccharose;
(iii) 0-10 wt% magnesium stearate;
(iv) 0-30 wt% cellulose;
(v) 0-10 wt% polyvinyl-pyrrolidone;
(vi) 0-10 wt% polymeric cellulose compounds;
(vii) 0-10 wt% highly dispersed silicon dioxide; and/or
(viii) 0-20 wt% cross-linked polyvinyl pyrrolidone.

(I) preferably has a disintegrant content of at least 5 wt% and the solid dosage form is coated with an aqueous film suspension (i.e. (III)).

Preparation: (I) is produced by (II).

Preferred Method: In (II), the MC of the (Ia) and (Ib) granulates is 10-15%. The BD is 0.4-0.75 g/ml. The pressed mass is processed into tablet using a tablet press and the tablets are then coated with an aqueous film suspension (i.e. (III)). Film coating is carried out with 30-50g of film suspension per minute during the first 30-70 minutes and then with 60-90g of film suspension per minute until the coating is complete.

ABEX ADMINISTRATION - Doses of (I) comprise 10-50 mg of (Ia) and 5-30 mg of (Ib). (I) is administered as a solid (claimed).

EXAMPLE - 64500 g of purified water were placed in a kettle and 15000 g of sieved lactose D80, 7500 g of sieved saccharose and 1500 g of polyvinylpyrrolidone 25000 (e.g. Kollidon 25 (RTM)) were added

to it and dissolved whilst stirring for 30 minutes. Subsequently, 3000 g of highly dispersed silicon dioxide (e.g. Aerosil 200 (RTM)) and 37500 g of finely crystalline carvedilol were added to the above solution and stirred for 30 minutes until a homogeneous suspension was produced. The suspension was pumped over a colloid mill and a hand sieve into a different container. The suspension was stirred continuously until the fluidized bed granulation had finished in order to prevent settling. - 30000 g of finely ground saccharose and 15000 g of cross-linked polyvinylpyrrolidone (e.g. Plasdone XL (RTM)) are placed in the pan of the fluidized bed granulator (e.g. GLATT - WSG 150 (RTM)). The suspension obtained under above was introduced using a tube pump. The spray granulation took place with an air supply temperature of about 80
degrees Centigrade and a product temperature of about 34
degrees Centigrade to 37 degrees Centigrade. The moisture content of the spent air amounted to 50 to 70% of the relative humidity, the spraying time amounts to about 120 minutes. - After the fluidized bed granulation the granulate was passed through a sieve with a mesh size of 1.2 mm. - 8250 g of cross-linked polyvinylpyrrolidone (e.g. Plasdone XL (RTM)) and 3000 g of highly dispersed silicon dioxide (e.g. Acrosil 200) were passed through a sieve with a mesh size of 1.2 mm and homogenized with the granulate in a mixer (e.g. a plowshare mixer from LODIGE). Then, 2250 g of magnesium stearate were passed through a sieve, with a mesh size of 1.2 mm and the sieved magnesium stearate was mixed briefly with the granulate and the granulate yield was established (target weight: 123000 g). Subsequently, the IPC values (IPC = in process control) of the final mixture were determined. - 1040 g of polyvinylpyrrolidone 25,000 (e.g. Kollidon 25 (RTM)) were dissolved in 9620 g of water while stirring. - 19500 g of hydrochlorothiazide and 28340 g of lactose were mixed in a mixer-granulator (e.g. DIOSNA (RTM)) for 4 minutes. 10660 g of the granulation solution was sprayed into the mixer with a spray pressure of 2 bar and granulated in the mixer-granulator for 5 minutes. The mist granulate was dried to a defined final moisture content at an air inlet temperature of 75 degrees Centigrade. - The dried granulate from above was passed through a pharma sieve with a mesh size of 1.25 mm and subsequently the granulate moisture was determined. Subsequently, the granulate weight was determined (target weight: 74880 g). - 15600 g of microcrystalline cellulose together with 7,280 g of cross-linked polyvinylpyrrolidone (e.g. Plasdone XL (RTM)), 2080 g of highly dispersed silicon dioxide (e.g. Aerosil 200 (RTM)) and 1040 g of magnesium stearate were passed through a pharma sieve with a mesh size of 1.25 mm. This sieved material and the sieved granulate from above were added to a pharma mixer and mixed for 30 seconds. The finished mixture is discharged into a pharma container and the yield was determined. Subsequently,

the IPC values of the final mixture were determined. - 70340 g of hydrochlorothiazide granulate and 120160 g of carvedilol granulate were placed in a suitable pharma mixer (e.g. plowshare mixer LODIGE) and homogeneously mixed. The mixing time was 3 minutes. The finished mixture was filled into an air-tight container through which light cannot pass and the yield was determined (target weight: 19500 g). Subsequently, the IPC values of the final mixture were determined. - The pressed mass was pressed using a computer-controlled high performance rotary tablet press (e.g. KILIAN TX 40 (RTM) with an automatic pressing force control and regulation of tablet weight) to tablets, which were stored in a container impervious to light.

L173 ANSWER 23 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2000-320296 [28] WPIX Full-text
ED 20050411
DNC C2000-097265 [28]
TI Detergent tablet useful for e.g. domestic laundry utilizes one of the cleaning components e.g. a photo-bleach to provide color to the colored layer
DC D25
IN ARNAU MUNOZ J; ARNAU-MUNOZ J; DEL MAR OLLERO N M; NOVO M D M O; OLLERO NOVO M D M; VEGA J L
PA (PROC-C) PROCTER & GAMBLE CO
CYC 88
PI EP 999261 A1 20000510 (200028)* EN 24[1]
<--
WO 2000027989 A1 20000518 (200032) EN
<--
AU 2000012372 A 20000529 (200041) EN
<--
BR 9915061 A 20010731 (200146) PT
<--
EP 1124934 A1 20010822 (200149) EN
<--
KR 2001075683 A 20010809 (200211) KO
<--
CN 1333816 A 20020130 (200231) ZH
<--
MX 2001004622 A1 20010701 (200236) ES
<--
CZ 2001001302 A3 20020515 (200241) CS
<--
JP 2002529586 W 20020910 (200274) JA 49
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ADT EP 999261 A1 EP 1998-870239 19981105; BR 9915061 A BR 1999-15061 19991027; CN 1333816 A CN 1999-815441

19991027; EP 1124934 A1 EP 1999-971843 19991027; WO 2000027989 A1 WO 1999-US25223 19991027; BR 9915061 A WO 1999-US25223 19991027; EP 1124934 A1 WO 1999-US25223 19991027; CZ 2001001302 A3 WO 1999-US25223 19991027; JP 2002529586 W WO 1999-US25223 19991027; AU 2000012372 A AU 2000-12372 19991027; JP 2002529586 W JP 2000-581156 19991027; CZ 2001001302 A3 CZ 2001-1302 19991027; KR 2001075683 A KR 2001-705673 20010504; MX 2001004622 A1 MX 2001-4622 20010507

FDT AU 2000012372 A Based on WO 2000027989 A; BR 9915061 A Based on WO 2000027989 A; EP 1124934 A1 Based on WO 2000027989 A; CZ 2001001302 A3 Based on WO 2000027989 A; JP 2002529586 W Based on WO 2000027989 A

PRAI EP 1998-870239 19981105

IC ICM C11D017-06

IPCR C11D0017-00 [I,A]; C11D0017-00 [I,C]; C11D0017-06 [I,A]; C11D0017-06 [I,C]; C11D0003-00 [I,A]; C11D0003-00 [I,C]; C11D0003-395 [I,A]; C11D0003-395 [I,C]; C11D0003-40 [I,A]; C11D0003-40 [I,C]

EPC C11D0003-00B12; C11D0017-00H8T2

AB EP 999261 A1 UPAB: 20050411

NOVELTY - A new detergent tablet comprises at least one colored layer, the color being produced by a component having a function in cleaning.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a process for producing the tablet. The process comprises:

(i) mixing the cleaning component with a nonionic carrier;

(ii) spraying the mixture onto a particulate product; and

(iii) compressing to form a tablet.

USE - Detergent tablet for domestic (e.g. laundry) use.

ADVANTAGE - The layered structure of detergent tablets is known to increase consumer acceptance of the product. The effect is usually obtained by adding dyes whose sole function is aesthetic improvement. This is costly, may result in laundry staining and produces an extra burden on the environment. The invention uses a cleaning component to produce the color.

TECH ORGANIC CHEMISTRY - Preferred Tablet: The tablet comprises at least two layers i.e. the colored layer and at least one other layer which may be white (or a different color). The white layer comprises a larger quantity of brightener than the other layer and is free of any colored component. The component with a cleaning function is a colored photo-bleach. The tablet is free of dye. The tensile strength of the tablet is less than 100 kPa. The tablet further comprises a binder.

ABEX EXAMPLE - A detergent base powder was prepared by mixing all the particulate materials apart from the binder spray-on system, the fluorescer or brightener, and the photo-bleach zinc phthalocyanine sulfonate. The particulate mixture was then divided in two equal

parts, one part for making a white layer, another part for making a green layer. The white layer material was obtained by spraying the brightener or fluorescer together with half of the binder. The green layer material was obtained by spraying the photo-bleach together with the rest of the binder. The layers where then processed independently in a Loedige KM 600 (RTM). - Using a Bonals (RTM) rotary press, both matrices were filled in two independent force feeding flasks. Both layers were compressed together in the precompression and compression stations to form a dual layer tablet. The resulting tablets had a square cross section of 45 mm a side, a height of 24 mm and a weight of 45 g. The height of the green bottom layer corresponded to 50% of the total height of the tablet. - The tablet was then coated with 2.5 g of coating formed from 80 wt.% of sebacic acid and 20 wt.% of Nymcel (RTM: carboxymethyl cellulose with degree of substitution 3). The color of the white layer of the coated tablet had the values: a = -2, b = 10, L = 85. The color of the green layer had the values: a = -9, b = 3, L = 80.

IT UPIT 20050411
106832-USE; 133912-USE; 133998-USE; 140011-USE; 140012-USE; 190069-USE; 232293-USE

FS CPI

MC CPI: D11-D03
DRN: 0924-U 1835-U
DCR: 106832-U 133912-U 133998-U 140011-U 140012-U 190069-U 232293-U

L173 ANSWER 24 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 2000-306008 [27] WPIX Full-text

ED 20050410

DNC C2000-093052 [27]

TI Multi-layer detergent tablet useful for e.g. domestic laundry has the layer effect imparted by one of the layers comprising a larger quantity of brightener than the other

DC D25

IN NOVO M D M O; OLLERO NOVO M D M; VEGA J L

PA (PROC-C) PROCTER & GAMBLE CO

CYC 88

PI EP 999262 A1 20000510 (200027)* EN 24[1]
<--
WO 2000027988 A1 20000518 (200032) EN
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AU 2000012371 A 20000529 (200041) EN
<--
BR 9915113 A 20010731 (200146) PT
<--
EP 1124933 A1 20010822 (200149) EN
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CN 1332793 A 20020123 (200231) ZH
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MX 2001004576 A1 20010701 (200236) ES
<--
JP 2002529585 W 20020910 (200274) JA 49
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ADT EP 999262 A1 EP 1998-870240 19981105; BR 9915113 A BR 1999-15113 19991027; CN 1332793 A CN 1999-815413 19991027; EP 1124933 A1 EP 1999-971842 19991027; WO 2000027988 A1 WO 1999-US25222 19991027; BR 9915113 A WO 1999-US25222 19991027; EP 1124933 A1 WO 1999-US25222 19991027; JP 2002529585 W WO 1999-US25222 19991027; AU 2000012371 A AU 2000-12371 19991027; JP 2002529585 W JP 2000-581155 19991027; MX 2001004576 A1 MX 2001-4576 20010504

FDT AU 2000012371 A Based on WO 2000027988 A; BR 9915113 A Based on WO 2000027988 A; EP 1124933 A1 Based on WO 2000027988 A; JP 2002529585 W Based on WO 2000027988 A

PRAI EP 1998-870240 19981105

IC ICM C11D017-06

IPCR C11D0011-00 [I,A]; C11D0011-00 [I,C]; C11D0017-00 [I,A]; C11D0017-00 [I,C]; C11D0017-06 [I,A]; C11D0017-06 [I,C]; C11D0003-00 [I,A]; C11D0003-00 [I,C]; C11D0003-40 [I,A]; C11D0003-40 [I,C]; C11D0003-42 [I,A]

EPC C11D0003-00B12; C11D0003-42; C11D0017-00H8T2

AB EP 999262 A1 UPAB: 20050410

NOVELTY - A new detergent tablet comprises at least two layers. One of the layers comprises a larger quantity of a brightener than the other layer.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a process for producing the tablet. The process comprises:

(i) forming a detergent composition matrix;

(ii) spraying the matrix with a brightener; and

(iii) compressing the matrix to a tablet.

USE - Detergent tablet for domestic (e.g. laundry) use.

ADVANTAGE - The layered structure of detergent tablets is known to increase consumer acceptance of the product. The effect is usually obtained by adding dyes whose sole function is aesthetic improvement. This is both costly and produces an extra burden on the environment. The invention provides a tonal contrast between the layers by varying their content of brightener

TECH ORGANIC CHEMISTRY - Preferred Tablet: The tablet comprises one colored layer, the color being produced by a component having a cleaning function (e.g. a colored photo-bleach). The colored layer is free of dye. The layer containing the larger quantity of brightener is free of any colored component. The tensile strength of the tablet is less than 100 kPa. The

tablet further comprises a binder and may be coated.
Preferred Production: The brightener is sprayed in the second step together with a nonionic carrier.

ABEX EXAMPLE - A detergent base powder was prepared by mixing all the particulate materials apart from the binder spray-on system, the fluorescer or brightener, and the photo-bleach zinc phthalocyanine sulfonate. The particulate mixture was then divided in two equal parts, one part for making a white layer, another part for making a green layer. The white layer material was obtained by spraying the brightener or fluorescer together with half of the binder. The green layer material was obtained by spraying the photo-bleach together with the rest of the binder. The layers where then processed independently in a Loedige KM 600 (RTM). - Using a Bonals (RTM) rotary press, both matrices were filled in two independent force feeding flasks. Both layers were compressed together in the precompression and compression stations to form a dual layer tablet. The resulting tablets had a square cross section of 45 mm a side, a height of 24 mm and a weight of 45 g. The height of the green bottom layer corresponded to 50% of the total height of the tablet. - The tablet was then coated with 2.5 g of coating formed from 80 wt.% of sebacic acid and 20 wt.% of Nymcel (RTM: carboxymethyl cellulose with degree of substitution 3). The color of the white layer of the coated tablet had the values: a = -2, b = 10, L = 85. The color of the green layer had the values: a = -9, b = 3, L = 80.

FS CPI
MC CPI: D11-D02

L173 ANSWER 25 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2000-100276 [09] WPIX
ED 20050705
CR 2000-100277; 2000-100278; 2000-161126; 2000-161127; 2000-163370; 2002-599229
DNC C2000-029305 [09]
TI Multi-phase detergent tablet for use in a dish washing or laundry washing machines
DC D16; D25; P71
IN BENNIE B F; BINDER C J; RICCI P
PA (PROC-C) PROCTER & GAMBLE CO
CYC 85
AB GB 2339790 A UPAB: 20060115
NOVELTY - Multi-phase detergent tablet for use in a washing machine comprises:
(a) a first phase in the form of a shaped body having at least one mold in it; and
(b) a second phase in the form of a particulate solid compressed within the mold.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the preparation of the multi-phase detergent tablet.

USE - The multi-phase tablet is used in automatic dishwashing or laundry washing machines.

ADVANTAGE - The tablet is robust enough to withstand handling and transportation. At least a portion of it dissolves rapidly in water providing rapid delivery of active agent.

TECH ENVIRONMENT - Preferred Tablet: The second phase is compressed at a pressure of less than 350 kg/cm2. The second phase dissolves more rapidly than the first phase. The second phase dissolves more rapidly than the first phase. The second phase dissolves in a dishwashing machine in 5 minutes.

The tablet contains at least one detergent active and is formulated such that at least 50 (preferably 80) wt. % of the detergent is delivered to the wash within 10 (preferably 3) minutes. The detergent active is selected from enzymes, bleaches, bleach activators, bleach catalysts, surfactants, chelating agents, and/or crystal growth inhibitors, and is predominantly concentrated in the second phase. The second phase additionally comprises a disrupting agent and/or an enzyme. The first and/or second phase may also comprise a binder. The binder is selected from sugar or starch or their derivatives, or inorganic or organic polymers. The tablet further comprises a barrier phase between the first and second phases. The barrier layer comprises a binder applied in liquid form.

Preparation: Claimed preparation of the tablet comprises:

(a) compressing a first detergent active composition to form a first phase comprising a mold;

(b) delivering a second detergent active composition in particulate form into the mold; and

(c) compressing the particulate detergent composition within the mold.

ABEX EXAMPLE - A two phase tablet system was prepared comprising, in phase 1: sodium tripolyphosphate (9.62); amorphous sodium silicate (0.50); crystalline layered silicate delta-Na2Si2O5 (1.5); amorphous sodium carbonate (2.33); ethane-1-hydroxy-1,1-diphosphonic acid (0.18); anhydrous sodium perborate monohydrate (2.45); pentaamine acetate cobalt (III) salt (0.002); amylase (0.148); protease (0.06); 13-15C mixed ethoxylated/propoxylated fatty alcohol with an average degree of ethoxyaltion of 3.8 and an average degree of propoxylation of 4.5 ('Plurafac' (RTM) ;0.40), polyethylene glycol (PEG) 6000 (0.4); benzotriazole (0.04); paraffin (0.10); and perfume (0.02); and in phase 2: amylase (0.30); protease (0.25); citric acid (0.3); sodium hydrogen carbonate (1.09); and PEG 3000 (0.06). - The detergent active composition of phase 1 was prepared by admixing the granular and liquid components and was then passed into the die of a rotary press. The

press included a punch shaped for forming the mold. The cross-section of the die was 30x38 mm. The composition was subjected to 940 kg/cm2 and the punch was elevated exposing the first phase of the tablet containing the mold in its upper surface. The detergent active composition of phase 2 was prepared in a similar manner and was passed into the die. The particulate active composition was then subjected to a compression force of 170 kg/cm2, the punch elevated and the multi-phase tablet ejected from the tablet press. - The resulting tablet dissolved in a washing machine within 12 minutes, phase 2 dissolving within 5 minutes. The tablets provided excellent dissolution and cleaning characteristics together with good tablet integrity and strength.

FS CPI; GMPI

MC CPI: A12-W12A; D05-A02; D11-A; D11-B01; D11-B02; D11-B03; D11-B06; D11-D01A; D11-D03

L173 ANSWER 26 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 1999-312552 [26] WPIX Full-text

ED 20050521

DNC C1999-092249 [26]

TI Effervescent base for preparation of effervescent tablet

DC B07; P32

IN GERGELY G; GERGELY I; GERGELY S; GERGELY T

PA (GERG-I) GERGELY G; (GERG-I) GERGELY I; (GERG-I) GERGELY S; (GERG-I) GERGELY T

CYC 22

PI WO 9920246 A1 19990429 (199926)* EN 17[6]
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EP 1024787 A1 20000809 (200039) EN
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BR 9813873 A 20000926 (200051) PT
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CN 1276716 A 20001213 (200118) ZH
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EP 1024787 B1 20020123 (200207) EN
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DE 69803594 E 20020314 (200226) DE
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CH 692439 A5 20020628 (200250) DE
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US 20020150614 A1 20021017 (200270) EN
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US 6497900 B2 20021224 (200303) EN
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CN 1203841 C 20050601 (200643) ZH

ADT WO 9920246 A1 WO 1998-EP6663 19981021; CH 692439 A5 CH 1997-2446 19971021; BR 9813873 A BR 1998-13873 19981021; CN 1276716 A CN 1998-810382 19981021; DE 69803594 E DE 1998-603594 19981021; EP 1024787 A1 EP 1998-956857 19981021; EP 1024787 B1 EP 1998-956857 19981021; DE 69803594 E EP 1998-956857 19981021; EP 1024787 A1 WO 1998-EP6663 19981021; BR 9813873 A WO 1998-EP6663 19981021; EP 1024787 B1 WO 1998-EP6663 19981021; DE 69803594 E WO 1998-EP6663 19981021; US 20020150614 A1 WO 1998-EP6663 19981021; US 6497900 B2 WO 1998-EP6663 19981021; US 20020150614 A1 US 2000-529343 20000524; US 6497900 B2 US 2000-529343 20000524; CN 1203841 C CN 1998-810382 19981021

FDT DE 69803594 E Based on EP 1024787 A; EP 1024787 A1 Based on WO 9920246 A; BR 9813873 A Based on WO 9920246 A; EP 1024787 B1 Based on WO 9920246 A; DE 69803594 E Based on WO 9920246 A; US 6497900 B2 Based on WO 9920246 A

PRAI CH 1997-2488 19971028
CH 1997-2446 19971021

IC ICM A61K009-00

IPCR A61K0009-46 [I,A]; A61K0009-46 [I,C]

EPC A61K0009-00L6

NCL NCLM 424/449.000

AB WO 1999020246 A1 UPAB: 20050521

NOVELTY - An effervescent base for the preparation of effervescent tablets and effervescent granules comprises at least one acid component formed by a mixture of (predominantly) monosodium tartrate and (possibly) disodium tartrate and one gas-evolving component, and optionally tartaric acid.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the preparation of the effervescent base.

USE - The use of the acid component of an effervescent system mixed with alkali hydrogen carbonate and/or carbonates has been found to be particularly advantageous for the incorporation of acid-sensitive active substances, such as H2-blockers for example ranitidine and famotidine.

ADVANTAGE - The tartaric acid, which is converted to monosodium tartrate, with sodium bicarbonate gives surprisingly short dissolution times and in particular is stable to atmospheric humidity of 80 % for 6 days or more. When the base incorporates an acid-sensitive active substance, there was found to be a lower tendency, especially also in a stress situation, on the part of the active substances to break down and to form decomposition products. The system is also suitable for alkali-sensitive active substances as it only requires small amounts of alkali hydrogen carbonates and/or carbonates in order to achieve rapid dissolution of the effervescent tablet.

TECH PHARMACEUTICALS - Preferred Base: The effervescent base additionally comprises an acid sensitive or an alkali-sensitive pharmaceutical. Preferred Preparation: The effervescent base is prepared by mixing tartaric acid with sodium bicarbonate and sodium carbonate containing water of crystallisation and slowly reacting at a temperature increasing to 50 0C, after which more sodium carbonate containing water of crystallisation is added and is allowed to react up to a temperature of 60 0C. Then drying is carried out, preferably in vacuo, the mixture is mixed with further, new, anhydrous sodium carbonate and the product is optionally pressed to give tablets.

ABEX EXAMPLE - Famotidine (40 parts by weight), tartaric acid effervescent system (1056 parts by weight), sodium bicarbonate (89 parts by weight), sodium carbonate (55 parts by weight), sodium cyclamate (30 parts by weight), saccharin sodium (3 parts by weight), mannitol (87 parts by weight) and a solid flavouring agent (40 parts by weight) were pressed to give famotidine effervescent tablets having a tablet weight of 1200 mg. The dissolution time was about 40 seconds and the pH was 4.5.

L173 ANSWER 27 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 1998-397429 [34] WPIX Full-text

ED 20050521

CR 1997-371686

DNC C1998-120241 [34]

DNN N1998-309164 [34]

TI Animal litter box with compacted bentonite-based absorbent - comprises water-swellable bentonite-containing material and suitable for absorbing animal urine

DC D22; P14

IN TUCKER E B

PA (FIRS-N) FIRST BRANDS CORP

CYC 1

PI US 5775259 A 19980707 (199834)* EN 17[0]
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ADT US 5775259 A CIP of US 1995-551190 19951031; US 5775259 A US 1997-890166 19970709

FDT US 5775259 A CIP of US 5647300 A

PRAI US 1997-890166 19970709
US 1995-551190 19951031

IPCR A01K0001-015 [I,A]; A01K0001-015 [I,C]

EPC A01K0001-015B2

AB US 5775259 A UPAB: 20060114
An animal litter comprises at least 5 wt.% of a water-swellable bentonite-containing material containing a compacted bentonite formed by compacting bentonite-containing particles, and contains at least one additive selected from: (a) sodium perborate (0.1-20 wt.%); (b)

dyes (urine activated colour dyes) (3000-12000 ppm, preferably 6000-10000 ppm); (c) citric acid and its salts (0.1-5 wt.%); (d) dye/sodium perborate (0.1-5 wt.%, ratio 1:5-1:50); (e) starch (0.5-5 wt.%, preferably 2-4 wt.%); (f) guar gum (0.5-2 wt.%, preferably 1-1.5 wt.%); (g) sodium or potassium bicarbonate (0.5-10 wt.%, preferably 2-25 wt.%); (h) citric acid or its salts (0.5-10 wt.%, preferably 2-25 wt.%); (i) water dispersible dye (FD&C Blue No. 1 (Brilliant Blue FCF), FD&C Green No. 3 (Fast Green FCF), Phloxine B (D&C Red 28) (3000-12000 ppm, preferably 6000-10000 ppm); (j) activated carbon or other carbonaceous absorbent (0.5-5 wt.%, preferably 1-3 wt.%); (k) zeolites and/or other molecular sieves (0.5-5 w t.%, preferably 1-3 wt.%); (l) spray dried fragrance (25% loading, 0.1-0.4 wt.%, 250-1000 ppm oil on a carrier); (m) pine-wood flour (2-20 wt.%, preferably 4-8 wt.%); (n) cedar-wood flour (2-20 wt.%, preferably 4-8 wt.%); and (o) spruce-wood flour (2-20 wt.%, preferably 4-8 wt.%), and mixtures of these. The bentonite-containing particles have an effective amount of the particles smaller than 100 US mesh. They have a moisture content = 5-15 wt.%, based on the total weight of water and bentonite. They are compacted under compacting pressure to form compacted masses, which are formed into particles of appropriate size for use as animal litter.

USE - The animal litter is used for absorbing animal urine, particularly for use in a litter box (claimed). It is particularly useful for smaller household animals such as cats. The absorbents can be used for a variety of other liquid absorbing applications.

ADVANTAGE - The litter provides an absorbency for animal urine greater than the comparable absorbency obtained from animal litter derived from a similar, non-compacted bentonite (claimed). It has good dry clump strength. The absorbents provide raw material cost savings over previous absorbents as they use the fines from other manufacturing processes.

ABDT US5775259

An animal litter comprises at least 5 wt.% of a water-swellable bentonite-containing material containing a compacted bentonite formed by compacting bentonite-containing particles, and contains at least one additive selected from: (a) sodium perborate (0.1-20 wt.%); (b) dyes (urine activated colour dyes) (3000-12000 ppm, preferably 6000-10000 ppm); (c) citric acid and its salts (0.1-5 wt.%); (d) dye/sodium perborate (0.1-5 wt.%, ratio 1:5-1:50); (e) starch (0.5-5 wt.%, preferably 2-4 wt.%); (f) guar gum (0.5-2 wt.%, preferably 1-1.5 wt.%); (g) sodium or potassium bicarbonate (0.5-10 wt.%, preferably 2-25 wt.%); (h) citric acid or its salts (0.5-10 wt.%, preferably 2-25 wt.%); (i) water dispersible dye (FD&C Blue No. 1 (Brilliant Blue FCF), FD&C Green No. 3 (Fast Green FCF), Phloxine B (D&C Red 28) (3000-12000 ppm, preferably 6000-10000 ppm); (j) activated carbon or other carbonaceous absorbent (0.5-5 wt.%, preferably 1-3 wt.%); (k) zeolites and/or other molecular sieves (0.5-5 w t.%, preferably 1-3 wt.%); (l) spray dried fragrance (25%

loading, 0.1-0.4 wt.%, 250-1000 ppm oil on a carrier); (m) pine-wood flour (2-20 wt.%, preferably 4-8 wt.%); (n) cedar-wood flour (2-20 wt.%, preferably 4-8 wt.%); and (o) spruce-wood flour (2-20 wt.%, preferably 4-8 wt.%), and mixtures of these. The bentonite-containing particles have an effective amount of the particles smaller than 100 US mesh. They have a moisture content = 5-15 wt.%, based on the total weight of water and bentonite. They are compacted under compacting pressure to form compacted masses, which are formed into particles of appropriate size for use as animal litter.

USE

The animal litter is used for absorbing animal urine, particularly for use in a litter box (claimed). It is particularly useful for smaller household animals such as cats. The absorbents can be used for a variety of other liquid absorbing applications.

ADVANTAGE

The litter provides an absorbency for animal urine greater than the comparable absorbency obtained from animal litter derived from a similar, non-compacted bentonite (claimed). It has good dry clump strength. The absorbents provide raw material cost savings over previous absorbents as they use the fines from other manufacturing processes.

EXAMPLE 1

A bentonite-containing material containing bentonite fines (59.1 wt.% less than 100 US mesh) were obtained from a commercial manufacturing process of a bentonite-based animal litter. The clumping animal litter formed from the natural bentonite was used as a control for comparison to the compacted bentonite of the invention. The bentonite was found to be a sodium bentonite with minor amounts of zeolite and calcium montmorrillonite. The moisture content of the control = 8.1 wt.%, bulk density = 61.6 lb/cu. ft. The moisture content of the fines = 7.5 wt.%, bulk density = 28.7 lb/cu.ft. (loose) and 71.8 lb/cu.ft. (tapped). The fines were fed to roll compacting equipment to form roll compacted sticks. A hydraulic pressure of 1300 psig was applied to form the compacted sticks at 280 lb/h. The compacted bentonite mass exhibited an average density = 1.84 g/cc. The compacted mass was fed to a comminutor to reduce the size to a granulated product of particle size range -12/+40 US mesh. Approximately 80% of the discharged comminuted product had a particle size larger than would pass through a 40 mesh screen. The moisture content of the comminuted product = 7.5 wt.% and the bulk density = 62.4 lb/cu.ft. The clump strength of the claimed product = 8.4 lbs, while that of the control = 4.1 lbs.

PREFERRED COMPONENTS

The water-swellable bentonite-containing materials are at least 30 wt.% fines from a manufacturing process for the manufacture of animal litter, the fines containing non-compacted bentonite. The

fines are derived from attrition during manufacturing of both compacted bentonite-containing absorbent and non-compacted bentonite absorbent. The animal litter contains at least 20 wt.% non-compacted bentonite and at least 20 wt.% compacted bentonite. It preferably comprises at least 50 wt.% bentonite-containing material, compacted from bentonite particles with at least 30 wt% of the particles having a size less than 100 US mesh and preferably at least 30 wt.% of the particles and more preferably at least 80 wt.% of the particles having a size less than 200 US mesh. The bentonite is preferably a sodium bentonite and is at least 50 wt.% montmorillonite. The bentonite particles are roll compacted between spaced apart rolls under a pressure of at least 5000, preferably at least 10000 and more preferably at least 20000 pounds/lineal inch. The compaction is performed under an effective compacting pressure of at least 1000 psig. Compaction may be effected by roll compaction, roll briquetting, vertical hydraulic pressing, flat plate pelletising, rotary tableting and gear pelleting. The compacting rollers may have surface designs that form cigar-shaped compacted bentonite-containing material. The bentonite to be compacted has a moisture content = 5-15 wt.% preferably 5-10 wt.%. The litter contains at least one additional absorbent material, selected from zeolites, fullers earth, attapulgite, diatomaceous earth, absorbent organic polymers, cellulosics and mixtures of these, and added at 5-60 wt.% of the animal litter. It further contains an additive selected from perfumes, deodorants, odour absorbents, antimicrobial agents, disinfectants, colourants, pesticides, pH-control agents, desiccants, perborates, chemical oxidants and mixtures of these. The compacted bentonite contains no adhesive binder.

PREFERRED PRODUCT

The animal litter formed has particles size distributions of 12/40, 8/25, 8/30, 12/30 or 16/40 US mesh range. The litter is capable of agglomerating on wetting into a clump of sufficient size and clump strength for physical removal either as a wet lump or after drying at room temperature for 24h.

IT UPIT 20060114

104520-USE; 107350-USE; 129792-USE; 129991-USE; 130395-USE; 132222-USE; 133510-USE; 140723-USE; 140725-USE; 159060-USE; 191428-USE; 2471-USE; 250717-USE; 278358-USE; 278359-USE; 3589-USE; 849-USE; 87079-USE; 95073-USE; 95095-USE; 99996-USE

FS CPI; GMPI

MC CPI: D09-C06

DRN: 0419-U 1698-U

DCR: 104520-U 107350-U 129792-U 129991-U 130395-U 132222-U 133510-U 140723-U 140725-U 159060-U 191428-U 2471-U 250717-U 278358-U 278359-U 3589-U 849-U 87079-U 95073-U 95095-U 99996-U

L173 ANSWER 28 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1997-503081 [46] WPIX
ED 20050703
DNC C1997-160016 [46]
DNN N1997-419294 [46]
TI Exothermic heat cell production using dry-compacted heating elements - comprising powdered iron, dry carbonaceous material and agglomeration aid with polyethylene@ cell forming material, for disposable body wrap
DC A96; D22; G04; P32
IN KEIM W R; WHITE R K
PA (PROC-C) PROCTER & GAMBLE CO
CYC 75
AB WO 1997036968 A1 UPAB: 20060113
Manufacturing exothermic heat cells comprises: (a) mixing a particulate exothermic composition comprising powdered iron, dry powdered carbonaceous material and an agglomeration aid to form an agglomeration;
(b) packing the agglomeration into a pocket formed between a bottom cell-forming surface and a top cell-forming surface, where at least one surface is oxygen permeable; preferably mixing a dry binder to the agglomeration to form an agglomerated pre-compaction composition; compacting and forming the pre-compaction composition into direct compaction articles selected from granules, pellets, tablets, slugs and mixtures; and packing the compaction articles into the pocket; and
(c) sealing the pocket forming a unified structure comprising opposed surfaces where the agglomeration or compaction article is sealed between the two surfaces.
The agglomeration or compaction article is activated by the addition of an aqueous solution, preferably 10-50 wt% of the agglomeration or compaction article, and the exothermic composition also comprises a metal salt added to the agglomeration or compaction article, or added subsequently as the aqueous solution.
USE - These heat cells are easily incorporated into disposable body wraps, such as for treatment of temporary or chronic pain.
ADVANTAGE - These disposable body wraps adapt to a wide variety of body contours, providing consistent, convenient and comfortable heat application. The densely compacted exothermic composition is easily wettable and gives extended heat generation. It is suitable for separate manufacture and distribution and provides a pre-measured dose size with no dust.

ABEQ (0010)
US 5984995 A UPAB 20060113
Manufacturing exothermic heat cells comprises:

(a) mixing a particulate exothermic composition comprising powdered iron, dry powdered carbonaceous material and an agglomeration aid to form an agglomeration;
(b) packing the agglomeration into a pocket formed between a bottom cell-forming surface and a top cell-forming surface, where at least one surface is oxygen permeable; preferably mixing a dry binder to the agglomeration to form an agglomerated pre-compaction composition; compacting and forming the pre-compaction composition into direct compaction articles selected from granules, pellets, tablets, slugs and mixtures; and packing the compaction articles into the pocket; and
(c) sealing the pocket forming a unified structure comprising opposed surfaces where the agglomeration or compaction article is sealed between the two surfaces.
The agglomeration or compaction article is activated by the addition of an aqueous solution, preferably 10-50 wt% of the agglomeration or compaction article, and the exothermic composition also comprises a metal salt added to the agglomeration or compaction article, or added subsequently as the aqueous solution.

USE - These heat cells are easily incorporated into disposable body wraps, such as for treatment of temporary or chronic pain.

ADVANTAGE - These disposable body wraps adapt to a wide variety of body contours, providing consistent, convenient and comfortable heat application. The densely compacted exothermic composition is easily wettable and gives extended heat generation. It is suitable for separate manufacture and distribution and provides a pre-measured dose size with no dust.

ABDT WO1997036968
A method of manufacturing exothermic heat cells comprises:
(a) mixing a particulate exothermic composition comprising powdered iron, dry powdered carbonaceous material and an agglomeration aid to form an agglomeration;
(b) packing the agglomeration into a pocket formed between a bottom cell-forming surface and a top cell-forming surface, where the surface(s) is oxygen permeable; preferably mixing a dry binder to the agglomeration to form an agglomerated pre-compaction composition; compacting and forming the pre-compaction composition into direct compaction articles selected from granules, pellets, tablets, slugs and mixtures; and packing the compaction articles into the pocket; and
(c) sealing the pocket forming a unified structure comprising opposed surfaces where the agglomeration or compaction article is sealed between the two surfaces.
The agglomeration or compaction article is activated by the addition of an aqueous solution, preferably 10-50 wt% of the agglomeration or compaction article, and the exothermic composition also comprises a metal salt added to the agglomeration or compaction article, or

added subsequently as the aqueous solution.
USE
The heat cells are easily incorporated into disposable body wraps, such as for treatment of temporary or chronic pain.
ADVANTAGE
The disposable body wraps adapt to a wide variety of body contours, providing consistent, convenient and comfortable heat application. The densely compacted exothermic composition is easily wettable and gives extended heat generation, and is suitable for separate manufacture and distribution and provides a pre-measured dose size with no dust.
EXAMPLE
Carbon (90 g) was mixed with sodium chloride (50 g) in a blender or mixer. Iron (620 g) and croscarmellose sodium (15 g) were added and mixed vigorously until the mixture was uniform. The mixture was sprayed with malitol syrup (60 g), while still being blended vigorously, to form a dust-free agglomeration. Gentle blending was used to mix acrylic acid-starch copolymer (15 g) into the agglomerated mixture. After this copolymer was dispersed uniformly, microcrystalline cellulose (150 g) was added. Gentle mixing was continued until all ingredients were distributed uniformly. The mixture was transferred to a rotary tablet press and compressed into disk-shaped tablets having a hole passing perpendicularly through the centre of the top and bottom surfaces. The tablets had a density of greater than 2.0 g/cm3, a thickness of 0.25 cm and a diameter of 2 cm. The tablet was added to the disk-shaped, vacuum-formed pocket in a sheet of LDPE film. A flat sheet of poly(ethylene-vinyl acetate) was placed over the LDPE sheet and the two sheets were heat-bonded together, such that the tablet was enclosed between the two sheets. Water was injected by needle through the polypropylene nonwoven/LDPE or /poly(ethylene vinyl acetate) sheet into the hole in the centre of the tablet, until the total water content was 20 wt% of the tablet composition.
The polypropylene nonwoven/LDPE sheet was perforated to provide a diffusive O2 permeability of 1.7 cc/min/5 cm2 (at 21°C, 1 atmosphere). The vacuum was released and the material around the heat cell was trimmed to provide a border of excess material around the perimeter of the cell. The cell began to generate heat shortly after the perforation of the LDPE film. The resulting cell height was 0.59 cm and the diameter was 2.1 cm, with a fill volume to cell volume ratio, after water had been added, of 0.89.
PREFERRED COMPOSITION
The exothermic composition comprises:
(a) 30-80% of iron powder;
(b) 3-20% of carbonaceous material of activated carbon, non-activated carbon or mixtures;
(c) 0-9% of an agglomeration aid of corn syrup, maltitol syrup,

crystallising sorbitol syrup, amorphous sorbitol syrup or mixtures; and
(d) 0-35% of a dry binder of microcrystalline cellulose, maltodextrin, sprayed lactose, co-crystallised sucrose and dextrin, modified dextrose, mannitol, microfine cellulose, pre-gelatinised starch, dicalcium phosphate, calcium carbonate or mixtures, preferably 4-30% of microcrystalline cellulose.
0.5-10% Metal salt of alkali metal salts, alkaline earth metal salts, transition metal salts and mixtures, preferably sodium chloride, is added to the composition as part of the dry mix or subsequently in a solution as brine, and the composition comprises 0.5-10% of additional water-holding materials of acrylic acid salt starch copolymer, isobutylene maleic anhydride copolymer, vermiculite, carboxymethylcellulose, or mixtures, and the composition has a physical form of dry agglomerated granules, direct compaction articles or mixtures.
The compaction articles are granules, pellets, tablets, slugs or mixtures.
The tablets and slugs have a geometric shape of disk, triangle, square, cube, rectangle, cylinder or ellipsoid, preferably they have a disk shaped geometry having a diameter of 0.2-10 cm and a height of 0.08-0.7 (0.1-0.15) cm and a density of greater than 1 (1.5-3.0) g/cm3 and preferably a cell volume of 0.0047-79 cm3.
Particularly the tablets have a disk shape where a hole passes perpendicular to and through the middle of the top and bottom surfaces, and the top and bottom surfaces are concaved, forming a reservoir conducive to holding a liquid.
The composition may further comprise:
(A) a unified structure comprising opposed surfaces of cell-forming materials, preferably films, nonwoven fabric laminated with a film layer substrate, web material comprising continuous filaments of thermoplastic resin laminated with a thermoplastic resin film, or mixtures, capable of forming a pocket using mechanical means, heat, vacuum or mixtures; and
(B) a shape of disk, triangle, pyramid, cone, sphere, square, cube, rectangle, rectangular parallelpiped, cylinder or ellipsoid.
The cell-forming materials are films of polyethylene, polypropylene, nylon, polyester, polyvinyl chloride, polyvinylidene chloride, polyurethane, polystyrene, saponified ethylene-vinyl acetate copolymer, ethylene-vinyl acetate copolymer, natural rubber, reclaimed rubber, synthetic rubber or mixtures.
The cell-forming material(s) are made air-permeable by perforating with aeration hole(s) having a diameter of 0.2-1 mm.

L173 ANSWER 29 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1997-371686 [34] WPIX Full-text
ED 20050518

CR 1998-397429
DNC C1997-119695 [34]
DNN N1997-308711 [34]
TI Absorbent comprising water-swellable bentonite of use in animal litter - is made by compacting fine bentonite particles, and then comminuting to form particles of suitable size
DC D22; P14
IN TUCKER E B
PA (FIRS-N) FIRST BRANDS CORP
CYC 25
PI US 5647300 A 19970715 (199734)* EN 18[0]
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EP 862853 A1 19980909 (199840)# EN
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CA 2198583 A 19980826 (199903)# EN
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CA 2198583 C 20030204 (200318)# EN
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ADT US 5647300 A US 1995-551190 19951031; CA 2198583 A CA 1997-2198583 19970226; CA 2198583 C CA 1997-2198583 19970226; EP 862853 A1 EP 1997-850033 19970304
PRAI US 1995-551190 19951031
CA 1997-2198583 19970226
EP 1997-850033 19970304
IPCR A01K0001-015 [I,A]; A01K0001-015 [I,C]
EPC A01K0001-015B2
AB US 5647300 A UPAB: 20050518
An absorbent comprises a water-swellable bentonite-containing material (I), formed by compacting bentonite-containing particles, an effective amount of which are smaller than 100 U.S. mesh, of moisture content 5-15 wt.%, to form a compacted mass, and forming the mass into particles of use as absorbent. Also claimed is an animal litter (II) containing at least 5 wt.% (I). Further claimed is the selective removal of waste from litter (II), by (a) contacting (II) with liquid animal waste to form clumps, and (b) removing the clumps from the remaining litter, either as wet clumps or after drying at room temperature.

USE - (I) is of general use for absorption of liquids, providing cost savings, and improved absorbency and performance. Particular use is in (II), e.g. in a cat litter box; it absorbs more animal urine than does non-compacted bentonite, forming clumps that are sufficiently strong to be removed mechanically from the remaining litter.

ABDT US5647300
An absorbent comprises a water-swellable bentonite-containing material (I), formed by compacting bentonite-containing particles, an effective amount of which are smaller than 100 U.S. mesh, of moisture content 5-15 wt.%, to form a compacted mass, and forming

the mass into particles of use as absorbent.
Also claimed is an animal litter (II) containing at least 5 wt.% (I).
Further claimed is the selective removal of waste from litter (II), by
(a) contacting (II) with liquid animal waste to form clumps, and
(b) removing the clumps from the remaining litter, either as wet clumps or after drying at room temperature.
USE
(I) is of general use for absorption of liquids, providing cost savings, and improved absorbency and performance. Particular use is in (II), e.g. in a cat litter box; it absorbs more animal urine than does non-compacted bentonite, forming clumps that are sufficiently strong to be removed mechanically from the remaining litter.
EXAMPLE
A bentonite-containing material containing bentonite fines (59.1% less than 100 mesh and 34.6% less than 200 mesh) was obtained from a bentonite based animal litter manufacturing process; the bentonite was largely sodium bentonite with minor amounts of zeolite and calcium montmorillonite; moisture was 8.1 wt.%, bulk density 61.6 lb/ft3. The fines were fed to a roll compactor operating at 1300 psig to form sticks, which were then comminuted to particle size -12/+40, and screened to 12/40 mesh, moisture 7.5%, bulk density 62.4. Clumps were formed by adding fresh cat urine and drying for 48 hours; in a testing machine, dry clump strength was 8.4 lbs, compared with 4.1 lbs for the starting material. (KKG)
PREFERRED ABSORBENT
The bentonite is sodium bentonite, at least 50 wt.% montmorillonite. Particles to be compacted contain 5-10 wt.% moisture, and optionally 5-60 wt.% additional absorbent material, e.g. zeolites, fullers earth, attapulgite, diatomaceous earth, absorbent organic polymers and/or cellulosics; they may include bentonite fines obtained in manufacture of an absorbent, e.g. by attrition during manufacture of bentonite-containing animal litter.
Compaction is by roll compaction, e.g. using spaced apart rolls at pressure at least 1000 (especially at least 20000) lb/lineal inch, or by roll briquetting, vertical hydraulic or flat plate pressing, rotary tabletting or gear pelleting.
Product is of particle size is 12/40 or 8/25 mesh; it may comprise at least 50 wt.% compacted bentonite and at least 30% particles of size less than 200 mesh, or at least 25% compacted and up to 75% non-compacted bentonite, with at least 30% of size less than 200 mesh. No adhesive binder is present.
PREFERRED LITTER
(I) contains at least 20% non-compacted and at least 20% compacted bentonite; it may additionally contain perfume, deodorant, odour absorbent, antimicrobial agent, disinfectant, colourant, pesticide,

pH control agent, desiccant, perborate and/or chemical oxidant. Particle size distribution may be 12/40, 8/25, 8/30, 12/30 or 16/40 or generally size suitable for use in a litter box. Absorbency for animal, e.g. cat, urine, is greater than that of litter containing non-compacted bentonite. It is capable of agglomerating on wetting in a litter box to form clumps sufficiently strong for physical removal from the box either when wet or after drying at room temperature for at least 24 hours.

FS CPI; GMPI

MC CPI: D09-A01

L173 ANSWER 30 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 1997-088062 [09] WPIX

ED 20050702

DNC C1997-028770 [09]

TI Multi layered medication tablet - has an outer covering layer to delay or block contact between the layered matrix core and a liquid medium for controlled release of the tablet ingredients

DC B07; P33

IN CKEMER K; CREMER K

PA (LOHM-C) LTS LOHMANN THERAPIE-SYSTEME AG; (LOHM-C) LTS LOHMANN THERAPIE-SYSTEME GMBH; (LOHM-C) LTS LOHMANN THERAPIE-SYSTEME GMBH & CO

CYC 32

AB DE 19524753 A1 UPAB: 20060201

The layered tablet, for the controlled release of the active ingredients in a liquid medium, has an outer covering layer to delay or block the ingredient release. It is applied by pressure on a layer of tablet ingredients on to the contact surfaces of a prepared tablet matrix, with different thicknesses, using powder or granule material. Or an additional layer is placed over a prepared covering layer. Also claimed is a mfg. process where a prepared compressed multi-layer tablet core is placed in the mould of a tablet prodn. machine. The powder or granule material for the covering layer, in the mould, is pressed in place round the matrix core, compressing the whole tablet structure.

USE - The tablet structure is used where the ingredients can be incompatible with each other, and where the tablet has a combination of therapeutic prescriptions with different actions and different release requirements into the patient's digestive system.

ADVANTAGE - The tablet gives a controlled release of its ingredients from a layered matrix, which can be produced on a conventional tablet press in a trouble-free operation.

ABEQ (0016)

US 6083533 A UPAB 20060201

The layered tablet, for the controlled release of the active ingredients in a liquid medium, has an outer covering layer to delay or block the ingredient release. It is applied by pressure on a layer of tablet ingredients on to the contact surfaces of a prepared tablet matrix, with different thicknesses, using powder or granule material. Or an additional layer is placed over a prepared covering layer. Also claimed is a mfg. process where a prepared compressed multi-layer tablet core is placed in the mould of a tablet prodn. machine. The powder or granule material for the covering layer, in the mould, is pressed in place round the matrix core, compressing the whole tablet structure.

USE - The tablet structure is used where the ingredients can be incompatible with each other, and where the tablet has a combination of therapeutic prescriptions with different actions and different release requirements into the patient's digestive system.

ADVANTAGE - The tablet gives a controlled release of its ingredients from a layered matrix, which can be produced on a conventional tablet press in a trouble-free operation.

ABDT DE19524753

The layered tablet, for the controlled release of the active ingredients in a liquid medium, has an outer covering layer to delay or block the ingredient release. It is applied by pressure on a layer of tablet ingredients on to the contact surfaces of a prepared tablet matrix, with different thicknesses, using powder or granule material. Or an additional layer is placed over a prepared covering layer.

Also claimed is a mfg. process where a prepared compressed multi-layer tablet core is placed in the mould of a tablet prodn. machine. The powder or granule material for the covering layer, in the mould, is pressed in place round the matrix core, compressing the whole tablet structure.

USE

The tablet structure is used where the ingredients can be incompatible with each other, and where the tablet has a combination of therapeutic prescriptions with different actions and different release requirements into the patient's digestive system.

ADVANTAGE

The tablet gives a controlled release of its ingredients from a layered matrix, which can be produced on a conventional tablet press in a trouble-free operation.

PREFERRED FEATURES

The dimensions of the contact surfaces of the layered matrix, to react with a liquid medium, are set by erosion of the covering layer thickness at defined points.

The covering layer has a multi-layer structure. The matrix is formed of layers of different ingredients as different materials and/or different medications. The matrix contact surfaces can be covered by different covering layers of different thicknesses and/or of materials which have different erosion behaviours. The matrix layers have different thicknesses, matching the thickness differences in the covering layer. The thickness differences shift continuously or with interruptions. The tablet ingredients are pharmaceuticals with a long dwell time in the stomach. The tablet is covered by a polymer film.

PREFERRED PRODUCTION

The tablets are produced on rotary tablet presses, with vacuum-charged transfer units to place prepared tablet cores in the moulds to form the finished multi-layered and coated tablets.

FS CPI; GMPI
MC CPI: B12-M10B; B12-M11K
CMC UPB 20060201
M6 *01* R038 R051 R052 R150 R511 R515 R522 R523 R531 M903

L173 ANSWER 31 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1997-054394 [06] WPIX Full-text
ED 20050702
DNC C1997-018116 [06]
TI Encapsulating core material e.g. food - by mixing with aq medium comprising natural polymer, treating at high pressure to form gel matrix and drying
DC A96; A97; B07; D13; P33
IN MANDRALIS Z I; TUOT J
PA (NEST-C) SOC PROD NESTLE SA
CYC 23
PI EP 750854 A2 19970102 (199706)* EN 7[3]
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ZA 9605532 A 19980325 (199819) EN 16
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MX 9602503 A1 19970601 (199825) ES
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BR 9602914 A 19990615 (199929) PT
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SG 74562 A1 20000822 (200049) EN
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CN 1141211 A 19970129 (200051) ZH
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RU 2164406 C2 20010327 (200130) RU
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EP 750854 B1 20011024 (200169) EN
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DE 69616167 E 20011129 (200202) DE

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ES 2164205 T3 20020216 (200222) ES
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TW 453893 A 20010911 (200242) ZH
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CN 1081946 C 20020403 (200516) ZH
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ADT EP 750854 A2 EP 1996-201691 19960618; DE 69616167 E DE 1996-69616167 19960618; DE 69616167 E EP 1996-201691 19960618; ES 2164205 T3 EP 1996-201691 19960618; BR 9602914 A BR 1996-2914 19960627; MX 9602503 A1 MX 1996-2503 19960627; CN 1141211 A CN 1996-111076 19960628; CN 1081946 C CN 1996-111076 19960628; RU 2164406 C2 RU 1996-112775 19960628; ZA 9605532 A ZA 1996-5532 19960628; SG 74562 A1 SG 1996-10180 19960629 ; TW 453893 A TW 1997-100673 19970122
FDT DE 69616167 E Based on EP 750854 A; ES 2164205 T3 Based on EP 750854 A
PRAI US 1995-672P 19950629
IC ICM A23P001-04; B01J013-02
IPCI A61J0003-07 [I,A]; A61J0003-07 [I,C]; A61K0009-50 [I,A]; A61K0009-50 [I,C]
IPCR A23L0001-00 [I,A]; A23L0001-00 [I,C]; A23L0001-025 [I,A]; A23L0001-025 [I,C]; A23L0001-22 [I,A]; A23L0001-22 [I,C]; A23L0001-27 [I,C]; A23L0001-275 [I,A]; A61K0009-16 [I,A]; A61K0009-16 [I,C]; B01J0013-02 [I,A]; B01J0013-02 [I,C]
EPC A23L0001-00P4; A23L0001-025; A23L0001-22B2; A23L0001-275; A61K0009-16H6H; A61K0009-16P4; B01J0013-02
AB EP 750854 A2 UPAB: 20050702
A process for encapsulating a core material comprises mixing the core material with an aq. medium comprising a natural polymer and treating the formed mixt at a pressure of 15000-200000 psi at 0-100°C to form a gel matrix comprising the core material encapsulated within the natural food polymer and drying. Before the pressure treatment, the formed mixt. is mixed with melted fat to form a water in oil emulsion contg. droplets, cooled to solidify the fat phase, then pressure treated to transform the droplets into gel particles which are separated from the fat phase and washed.
The core material is mixed with the aq. polymer medium by dissolving, emulsifying or dispersing it into an aq. soln. or dispersion or slurry of the polymer. The temp of the high pressure treatment is 15-60°C and is carried out in a hydrostatic press. Before the high pressure treatment, the mixt of the core material with the food polymer is sealed in a flexible bag made of rubber or plastic material. The duration of the high pressure treatment is 1-60 min. The core material is a flavour, colour, vitamin, mineral, spice, oil or pharmaceutical and is heat or chemically sensitive. The polymer

encapsulating material is whey protein, casein gelatin, human serum albumin, egg white, soy isolate, pectin or CMC.

USE - The process is useful for encapsulating sensitive food components to insure against nutritional loss and to mask or preserve flavours and aromas. - Encapsulation also increases the stability of vitamin or mineral supplements normally sensitive to UV light, oxygen, humidity and temp. and is used in the pharmaceutical industry to protect the lining of the mouth or oesophagus from harsh orally administered drugs or for controlled release of drugs delivered through intramuscular, subcutaneous or intravenous routes.

ADVANTAGE - The process avoids the disadvantages of the use of heat and chemicals by using a natural polymer as the encapsulating material.

ABDT EP750854

A process for encapsulating a core material comprises mixing the core material with an aq. medium comprising a natural polymer and treating the formed mixt at a pressure of 15000-200000 psi at 0-100°C to form a gel matrix comprising the core material encapsulated within the natural food polymer and drying.

USE

The process is useful for encapsulating sensitive food components to insure against nutritional loss and to mask or preserve flavours and aromas.

Encapsulation also increases the stability of vitamin or mineral supplements normally sensitive to UV light, oxygen, humidity and temp. and is used in the pharmaceutical industry to protect the lining of the mouth or oesophagus from harsh orally administered drugs or for controlled release of drugs delivered through intramuscular, subcutaneous or intravenous routes.

ADVANTAGE

The process avoids the disadvantages of the use of heat and chemicals by using a natural polymer as the encapsulating material.

EXAMPLE

Whey protein (Bi-Pro (RTM) 95%) (25 pts.) were dissolved in water (100 pts.) and micronutrient vitamin premix (0.06 pts.) added. The pH was adjusted to 5 and 7. The soln. was placed in a flexible pouch and pressurised at room temp. at 60000 psi for 20 min. The prod. gel matrix was ground and vacuum dried.

All the vitamins E and B1 survived the treatment at both pH levels. The texture of the denatured protein at pH 7 was more elastic, glossy and transparent than that of pH 5 which was more brittle and opaque. (SCG)

PREFERRED PROCESS

Before the pressure treatment, the formed mixt. is mixed with melted fat to form a water in oil emulsion contg. droplets, cooled to solidify the fat phase, then pressure treated to transform the droplets into gel particles which are separated from the fat phase

and washed.
The core material is mixed with the aq. polymer medium by dissolving, emulsifying or dispersing it into an aq. soln. or dispersion or slurry of the polymer. The temp of the high pressure treatment is 15-60°C and is carried out in a hydrostatic press. Before the high pressure treatment, the mixt of the core material with the food polymer is sealed in a flexible bag made of rubber or plastic material. The duration of the high pressure treatment is 1-60 min.
After the high pressure treatment the gel matrix is dried then ground or ground and dried to form capsules of the desired particle size. The amt of core material in the mixt. with the aq. natural polymer medium is 0.5-15 wt% based on the total wt. of the mixt and the amt. of polymer in the aq. medium is 1-50 wt% based on the total wt. of the aq. medium.
PREFERRED MATERIALS
The core material is a flavour, colour, vitamin, mineral, spice, oil or pharmaceutical and is heat or chemically sensitive.
The polymer encapsulating material is whey protein, casein gelatin, human serum albumin, egg white, soy isolate, pectin or CMC.
The polymer material is water-insol. after the high pressure treatment.

L173 ANSWER 32 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1996-019833 [02] WPIX Full-text
ED 20050510
CR 1991-202078; 1995-021210
DNC C1996-006788 [02]
TI Directly compressible compsn. contg. naproxen or naproxen sodium - obtained by spray-drying of aq. soln. to specified water content and mixing with binder, disintegrating agent and lubricant
DC A96; B05
IN CHOWHAN Z T; HAFEZZADEH H; KURAMOTO R; PENDLETON R O
PA (SYNT-C) SYNTEX PHARM INT LTD
CYC 1
PI US 5470580 A 19951128 (199602)* EN 8[0]
<--
ADT US 5470580 A Cont of US 1989-455109 19891222; US 5470580 A CIP of US 1991-759783 19910827; US 5470580 A Div Ex US 1992-878145 19920504; US 5470580 A US 1994-271339 19940706
FDT US 5470580 A Div ex US 5358717 A
PRAI US 1994-271339 19940706
US 1989-455109 19891222
US 1991-759783 19910827
US 1992-878145 19920504
IPCR A61K0031-185 [I,C]; A61K0031-19 [I,A]; A61K0009-14 [I,A];

A61K0009-14 [I,C]; A61K0009-16 [I,A]; A61K0009-16 [I,C]; A61K0009-20 [I,A]; A61K0009-20 [I,C]

EPC A61K0009-14; A61K0009-16H6B; A61K0009-16H6F; A61K0009-20H6F2; A61K0009-20P; A61K0031-19

AB US 5470580 A UPAB: 20050510

Directly compressible compsn. comprises: (a) 90-97% spray dried naproxen (I), 0.5-1.5% free moisture (M), 1-6% binder (B), 1-6% disintegrating agent (D) and 0.1-2% lubricant (L); or (b) 80-90% spray dried naproxen sodium (II), 6-8% M, 1-6% B, 1-6% D and 0.1-2% L.

Also claimed is an aq. mixt. for spray drying contg. 20-70% solids comprising 90.46-100% (I), 0-6.259. B, and 0-6.25% D or 85.11-100% (II), 0-6.97% B and 0-6.97% D; and a process for prepg. a tablet comprising (1) spray drying the aq. mixt.; (2) combining with water and dry excipients to obtd. a compsn. (a) or (b); and (III) compressing into a tablet:

ADVANTAGE - The compsns. are free flowing and possess good compactibility and compressibility characteristics. They are stable and can be packed in moisture-proof containers and stored for periods of time prior to tabletting. The tablets are stable and have good dissoln. characteristics. The spray dried prods. are prepd. from aq. mixture which does not require the energy intensive drying and milling steps of prior art. ABDT US5470580

Directly compressible compsn. comprises:

(a) 90-97% spray dried naproxen (I),

0.5-1.5% free moisture (M),

1-6% binder (B),

1-6% disintegrating agent (D) and

0.1-2% lubricant (L); or

(b) 80-90% spray dried naproxen sodium (II),

6-8% M,

1-6% B,

1-6% D and

0.1-2% L.

Also claimed are

(A) an aq. mixt. for spray drying contg. 20-70% solids comprising 90.46-100% (I), 0-6.25% B, and 0-6.25% D or 85.11-100% (II), 0-6.97% B and 0-6.97% D;

(B) a spray dried compsn. for combining with dry excipients to obtain a directly compressible compsn. comprising (a) 90-100% (I), 0-1.63% M, 0-6.25% BD and 0-6.25% DA; or (b) 80-100% (II), 0-9.0% M, 0-6.97% BD and 0-6.97% DA;

(C) a process for preparing a compsn. (a) or (b) by

(1) spray drying the aq. mixt.; and

(2) combining with water and dry excipients;

(D) a process for forming a tablet comprising steps (1) and (2), and

(3) compressing into a tablet:

A tablet contg. <97% spray dried (I) 0.5-1.5% M, 1-6% BD, 1-6% DA and 0.1-2% LB or 80-90% spray dried (II), 6-8% M, 1-6% BD, 1-6% DA and 0.1-2% LB is also claimed.

ADVANTAGE

The compsns. are free flowing and possess good compactibility and compressibility characteristics. They are stable and can be packed in moisture-proof containers and stored for periods of time prior to tabletting. The tablets are stable and have good dissoln. characteristics. The spray dried prods. are prepd. from aq. mixture which does not require the energy intensive drying and milling steps of prior art.

EXAMPLE

A directly compressible naproxen compsn. is prepd. from 35.0 kg (I), 1.4 kg croscarmellose sodium, 0.7 kg Povidone, K-90 and 37.1 kg water. The mixture is spray dried, using a silicate 2-fluid nozzle with a 2mm dia. orifice at nozzle air pressure of 4 psig., main inlet air temp. 239° C, fluid bed inlet temp. 88° C and outlet air temp. 66° C. The spray dried compsn. is blended with magnesium stearate to give a compsn. comprising 92% (I), 1.6% M, 4% croscarmellose sodium, 2% povidone K-90 and 0.2% magnesium stearate.

The prod. has mean particle size 100-350μ-m, good flow through a hopper and is compressible on a rotary tablet press to 5 S.C.Units under a 600-800 lb load and 10-18 S.C.Units under a 5200 lb compression load. (LJ)

PREFERRED EMBODIMENT

DA is croscarmellose sodium ad BD is povidone or HPMC pref. used at 2-6 and 1-4%.

L173 ANSWER 33 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1995-374952 [49] WPIX
ED 20050513
DNC C1995-162417 [49]
TI Tablets for controlling cold and flu symptoms - have menthol-flavoured coating, giving temporary relief of coughs and sore throats
DC A96; B05; B07
IN SONLEY C R; TURNBULL M A
PA (JOHJ-C) JOHNSON & JOHNSON; (MCNI-C) MCNEIL-PPC INC
CYC 25
AB EP 679391 A2 UPAB: 20050513

Solid, oral compsn. (I) for temporary relief of coughs and sore throats comprises: (a) a solid core contg. an analgesic and an antitussive; and (b) a methanol-flavoured film coating comprising a water soluble, film-forming to provide sensory stimulation of the throat and nasal passages when the compsn. is taken. The analgesic is

pref. acetaminophen and the antitussive is pref. dextromethorphan HBr.

The coating comprises pref. hydroxypropyl methylcellulose and a plasticiser and natural or artificial mint or peppermint flavour, menthol crystals, anise oil, eucalyptus oil or mixts.. The coating comprises 1-10wt.% total wt. of (I).

USE - The active ingredients in (I) are effective in combatting the symptoms of colds and flue, while the menthol coating provides the additional advantage of soothing sore throats and coughs for ≥ 10 seconds (pref. 2 mins.) and is pref. sweetener-free.

ABDT EP679391

Solid, oral compsn. (I) for temporary relief of coughs and sore throats comprises:

(a) a solid core contg. an analgesic and an antitussive; and

(b) a methanol-flavoured film coating comprising a water soluble, film-forming to provide sensory stimulation of the throat and nasal passages when the compsn. is taken.

USE

The active ingredients in (I) are effective in combatting the symptoms of colds and flue, while the menthol coating provides the additional advantage of soothing sore throats and coughs for ≥ 10 seconds (pref. 2 mins.) and is pref. sweetener-free.

EXAMPLE

Modified starch was sprayed on to a fluidised bed of acetaminophen (68.87%), dextromethorphan HBr (3.81%), powdered cellulose (6.38%), pregelatinised corn starch (3.06%) and sodium starch glycolate (2.78%) to give a dry granulate which was dry blended with microcrystalline cellulose (4.25%) and magnesium stearate (0.45%). This mixt. was compressed in a rotary tablet press into caplet-shaped tablets. The caplet cores (10 kg) were coated in a coating pan rotating at 12 rpm with a coating comprising hydroxypropyl methylcellulose (9.6%), peppermint (2.4%), natural and artificial mint flavour (1.7%) and purified water (86.3%) applied using an air atomised sprayer.

On completion of the coating the caplet bed was waxed by sprinkling with powdered carnauba wax (0.003%) and rotating until uniform. (SCG)

SR:No-SR.Pub

PREFERRED MATERIALS

The analgesic is pref. acetaminophen and the antitussive is pref. dextromethorphan HBr.

The coating comprises pref. hydroxypropyl methylcellulose and a plasticiser and natural or artificial mint or peppermint flavour, menthol crystals, anise oil, eucalyptus oil or mixts..

The coating comprises 1-10wt.% total wt. of (I).

(I) contains per tablet, e.g. 160-500mg acetaminophen, 7.5-15 mg dextromethorphan HBr, 0-30 mg pseudoephedrine HCl and 0-2 mg

chlorpheniramine maleate.

L173 ANSWER 34 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1995-303430 [40] WPIX
ED 20050702
DNC C1995-135762 [40]
TI Effervescent granules and tablets for oral admin. of hydrophobic pharmaceuticals - contg. grains of acid coated with neutral substance and having alkali component applied to this coating, dissolve rapidly and have low acid binding capacity
DC A96; B07
IN GERGELY G; GERGELY I; GERGELY S; GERGELY T
PA (GERG-I) GERGELI G; (GERG-I) GERGELY G
CYC 65
AB EP 670160 A1 UPAB: 20050702
Granular effervescent particles for producing an aq. soln. or suspension of at least one pharmaceutical (I) for oral admin. and which can be compressed into tablets comprises grains prepd. from carrier crystals of at least one solid, edible organic acid (II), coated by a water-soluble neutral substance (III) that lowers the m.pt. of (II) at the surface. At least one alkali(ne earth) (bi)carbonate or alkali(ne earth) salt of (II) is applied to this coating. Tablets made from these grains are included.
Also new are effervescent tablets in which carrier crystals of (II) have at least 2 coating layers: the first of another (II) and/or its salt, including as (III), a water-soluble polymer, higher alcohol, carbohydrate hydrocolloid, and the second comprising an alkali salt of (II). The tablet also contains an alkali metal (bi)carbonate. Other opt. ingredient are (1) if (I) is hydrophobic, a hydrophobic substance on a suspending agent or neutral substance, formulated as separate granules; and (2) binders (esp. PVP); surfactants (e.g. Na lauryl sulphate) and alkali(ne earth) (bi)carbonates.
USE - The granules are used to deliver hydrophobic (esp. also acid-sensitive) (I), esp. cimetidine, cisapride, β-carotene and ranitidine.
ADVANTAGE - Hydrophobic (I) can now be administered in effervescent liq. that are pleasant to drink. The compsns. have low acid-binding capacity (so have reduced antacid effects); dissolve quickly and, since (I) is not directly in contact with (II), have good storage stability.
ABDT EP670160
Granular effervescent particles for producing an aq. soln. or suspension of at least one pharmaceutical (I) for oral admin. and which can be compressed into tablets comprises grains prepd. from carrier crystals of at least one solid, edible organic acid (II), coated by a water-soluble neutral substance (III) that lowers the m.pt. of (II) at the surface. At least one alkali(ne earth)

(bi)carbonate or alkali(ne earth) salt of (II) is applied to this coating. Tablets made from these grains are included.
Also new are effervescent tablets in which carrier crystals of (II) have at least 2 coating layers: the first of another (II) and/or its salt, including as (III), a water-soluble polymer, higher alcohol, carbohydrate hydrocolloid, and the second comprising an alkali salt of (II). The tablet also contains an alkali metal (bi)carbonate.
USE
The granules are used to deliver hydrophobic (esp. also acid-sensitive) (I), esp. cimetidine, cisapride, β-carotene and ranitidine.
ADVANTAGE
Hydrophobic (I) can now be administered in effervescent liq. that are pleasant to drink. The compsns. have low acid-binding capacity (so have reduced antacid effects); dissolve quickly and, since (I) is not directly in contact with (II), have good storage stability.
PREPARATION
Crystals of (I) are wetted with aq. soln. of (III), then before they are completely dry, uniformly coated with powdered alkali(ne earth) (bi)carbonate. The grains are dried, mixed with (I) and adjuvant and opt. compressed into tablets.
Additional components may be introduced by wetting the granules with buffer soln. and/or the granules are mixed with granules contg. other materials. (I) may be combined with a neutral substance, suspending agent or carbonate component.
Opt. the surface of the acid and/or alkali component is passivated by treatment (while heating under vacuum) with a polar solvent that causes release of CO2 and contains (III). The treatment may be repeated until passivation is achieved.
Alternatively, portions of (II) and carbonate are prereacted in water and/or ethanol, and the product (mixed with (III)) mixed with crystalline (II) which thus becomes coated. Additional coatings contg. carbonate are then applied.
EXAMPLE
102 pts. (by wt.) coarse citric acid (IIa) and 25 pts. finely powdered (IIa) were added to a vacuum tank at 60°C, then 0.85 pts. soln. made from 36 pts. each water and sorbitol, 21 pts. (IIa) and 7 pts. NaHCO3 mixed in. These were followed by 52.5 pts. NaHCO3 and 4.4 pts. aspartame, then the particles were dried at 200 mbar and 1.9 pts. NaHCO3 added. After drying at 15 mbar a further 0.6 pt. soln. was added, the drying step was repeated, 9.3 pt. Na2CO3 added, and the final product dried and sieved.
Separately 7.7 pts. sorbitol powder were heated to 50°C then 0.2 pt. simethicone added in butanone-acetone and the mixt. dried at 15 mbar/45°C.
20 pts. (Ia) and 21.1 pts. sorbitol powder were mixed for 10 min., then 178.4 pt. of the effervescent granules, 7 pts. antifoam

granules and 4.5 pts. lemon flavour mixed in for 5 min. The final mixt. was compressed into 2.3g tablets, each contg. 0.2g (Ia) and of hardness 6-8 kp. (RMH)

PREFERRED GRANULES

(II) is present at 0.05-1 (pref. 0.07-0.8) wt.% and the granules may also include a moisture binding agent (Na2CO3 or Na2SO4 at 4-10 wt.% of total); additional coating of (II) salt as buffer; and pref. an antifoam (in one of the coating layers or in separate granules), esp. dimethicone or simethicone at 0.005-0.05% in total or 0.05-2 wt.% or (I).

Other opt. ingredient are (1) if (I) is hydrophobic, a hydrophobic substance on a suspending agent or neutral substance, formulated as separate granules; and (2) binders (esp. PVP); surfactants (e.g. Na lauryl sulphate) and alkali(ne earth) (bi)carbonates.

The granules (or tablets) have acid binding capacity (after USP 22) below 5 (esp. 3) mequiv., and for a total wt. not over 2.5 (esp. 2)g will dissolve in water at room temp. in below 180 (esp. 120) sec.

PREFERRED COMPOSITION

A typical formula (by wt.) is 2-30% cimetidine (Ia); 3-60% (II); 12-40% alkali(ne earth) (bi)carbonate (of which 2-10% is Na2CO3 as moisture binding agent); 1-4% sweetener; 0.01-30% neutral substance (of which 0.01-0.05% is in the coating); 3-20% sorbitol; 2-10% mannitol; 0.005-0.5% antifoam and 0.1-3% flavouring.

Formulae for the other pref. (I) are also given.

L173 ANSWER 35 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1995-075418 [10] WPIX
ED 20050702
DNC C1995-033552; C1995-096460 [10] [28]
TI Prepn. of stable steroid contg. granules - comprises dissolving steroid and lubricant in organic solvent, mixing obtd. soln. with diluent and binder and removing solvent while blending
DC A96; B01; B07; P33
IN DOPPER J H; VAN D V C J M; VAN DER VEN C J M; YAN H D
PA (ALKU-C) AKZO NOBEL NV; (ALKU-C) AKZO NV
CYC 27
AB ZA 9309337 A UPAB: 20060131

Prepn. of steroid loaded granules comprises (a) dissolving the steroid and a lubricant in an organic solvent, (b) mixing the soln. with diluent and binder and (c) removing the solvent while blending the mixt.. Also claimed is the granule contg. a film coating of the steroid and lubricant.

The steroid is pref. desogestrel and the lubricant is stearic acid. The granule comprises a carrier comprising lactose, polypyrrolidone and disintegrating agent and a film coating comprising desogestrel and stearic acid.

ADVANTAGE - Certain steroids (e..g desogestrel) transfer from tablets into the surrounding local environment. This can reduce the dose of steroid which is admin.. The granule retains at least 90% (pref. 98%) of the desogestrel at 150 mbar and 70°C for 72 hrs. (Reissue of the entry advised in week 9506 based on complete specification).

ABEQ (0002)
US 5395627 A UPAB 20060131
Granules used in tabletting comprises: (a) a carrier comprising lactose, polyvinylpyrrolidone and disintegrating agent, and (b) a film coating the carrier. The film comprises desogestrel and stearic acid, or desogestrel, diluent, binder and lubricant. The diluent is pref. lactose or mannitol. The disintegrating agent is corn starch, potato starch and/or wheat starch. The binder is polyvinylpyrrolidone or hydroxypropylcellulose. The lubricant is stearic acid.

USE/ADVANTAGE - Prodn. of pharmaceutical granulates. Transfer of desogestrel from tablets is prevented.

ABDT ZA9309337
Prepn. of steroid loaded granules comprises (a) dissolving the steroid and a lubricant in an organic solvent, (b) mixing the soln. with diluent and binder and (c) removing the solvent while blending the mixt..
Also claimed is the granule contg. a film coating of the steroid and lubricant.
ADVANTAGE
Certain steroids (e..g desogestrel) transfer from tablets into the surrounding local environment. This can reduce the dose of steroid which is admin.. The granule retains at least 90% (pref. 98%) of desogestrel at 150 mbar and 70°C for 72 hrs..
EXAMPLE
A vacuum mixer was charged with carrier components (87% lactose, 10% corn starch, 3% PVP, 4880 g) and heated to 35°C. Desogestrel (11.54 g), ethynyl estradiol (2.31 g), stearic acid (50 g) and dl-alpha-tocopherol (6.17 g) were dissolved in acetone (350 ml) and heated to 45°C. The soln. was added to the carrier at 100 mbar and the mixt. was blended for 10 mins. Blending was stopped and the mass was allowed to cool to 15°C, the vacuum increased to 25 mbar and the mixt. heated to 45°C while blending. The mixt. was further blended while the mass cooled to 20°C. Colloidal SiO_2 (50 g) was added and the mixt. was compressed on a rotary press to give tablets weighing 65 mg and contg. desogestrel (150 µg), ethynyl estradiol (30 µg) and dl-alpha-tocopherol (80µg). After 72 hrs. at 150 mbar and 70°C, the granules retained 97% desogestrel and the tablets 98% desogestrel. (TF)

PREFERRED METHOD
The steroid is desogestrel and the lubricant is stearic acid. The granule comprises a carrier comprising lactose, polypyrrolidone and disintegrating agent and a film coating comprising desogestrel and stearic acid.

L173 ANSWER 36 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1995-062091 [09] WPIX Full-text
ED 20050702
DNC C1995-027493 [09]
TI New rapidly disintegrating pharmaceutical dosage form - contg. pharmaceutical particles coated with a taste-masking compsn., a water-disintegratable, compressible carbohydrate and a binder
DC A96; B07
IN GOWAN W G
PA (JOHJ-C) JOHNSON & JOHNSON; (MCNI-C) MCNEIL-PPC INC
CYC 21
PI EP 636364 A1 19950201 (199509)* EN 10[0]
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CA 2128820 A 19950128 (199516) EN
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BR 9402962 A 19950411 (199521) PT
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US 5876759 A 19990302 (199916) EN
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EP 636364 B1 20000920 (200047) EN
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DE 69425932 E 20001026 (200061) DE
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ES 2152966 T3 20010216 (200114) ES
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MX 202606 B 20010625 (200235) ES
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ADT EP 636364 A1 EP 1994-305533 19940727; US 5876759 A Cont of US 1993-97806 19930727; CA 2128820 A CA 1994-2128820 19940726; BR 9402962 A BR 1994-2962 19940727; DE 69425932 E DE 1994-69425932 19940727; DE 69425932 E EP 1994-305533 19940727; ES 2152966 T3 EP 1994-305533 19940727; MX 202606 B MX 1994-5729 19940727; US 5876759 A Cont of US 1995-566649 19951204; US 5876759 A US 1997-842597 19970416
FDT DE 69425932 E Based on EP 636364 A; ES 2152966 T3 Based on EP 636364 A
PRAI US 1993-97806 19930727
US 1995-566649 19951204
US 1997-842597 19970416
IC ICM A61K009-20

IPCR A61K0009-00 [I,A]; A61K0009-00 [I,C]; A61K0009-20 [I,A]; A61K0009-20 [I,C]
EPC A61K0009-00M18B; A61K0009-20K2B
AB EP 636364 A1 UPAB: 20050702
A new compressed pharmaceutical dosage form comprises: at least one coated particle comprising at least one pharmaceutical coated with a taste-masking coating: a H2O-disintegratable, compressible carbohydrate; and a binder.
The dosage form has a hardness sufficient to cause the carbohydrate to disintegrate within 30 seconds after oral admin., allowing the particle to be swallowed.
Also claimed is a process for prepn. of the compsns..
USE - The dosage form may be a compressed wafer. The compsns. are available for human patients who have difficulty swallowing conventional tablets or capsules, and for the sublingual and buccal admin. of drugs.
ADVANTAGE - The compsns. have no objectionable taste. ABDT
EP636364
A new compressed pharmaceutical dosage form comprises: at least one coated particle comprising at least one pharmaceutical coated with a taste-masking coating: a H2O-disintegratable, compressible carbohydrate; and a binder.
The dosage form has a hardness sufficient to cause the carbohydrate to disintegrate within 30 seconds after oral admin., allowing the particle to be swallowed.
Also claimed is a process for prepn. of the compsns..
USE
The dosage form may be a compressed wafer. The compsns. are available for human patients who have difficulty swallowing conventional tablets or capsules, and for the sublingual and buccal admin. of drugs.
ADVANTAGE
The compsns. have no objectionable taste.
EXAMPLE
A coating soln. contg. a blend of cellulose acetate and polyvinyl pyrrolidone was prepd. at 12% solid with an acetone/CH3OH (80:20) solvent. The ratio of cellulose acetate to polyvinyl pyrrolidone was 85:15.
Acetaminophen (4kg) was placed in a fluidised state by a flow of air at a temp. of 30°C. The coating soln. was then sprayed (atomisation air pressure = 3 bar) onto the fluidised particles at a rate of 80g/min. until a coated acetaminophen particle contg. approx. 12% by wt. of the coating was obtd..
Colour (0.9mg/wafer) was screened through a 60 mesh screen, the coated acetaminophen (91.0 mg/water) was screened through a 30 mesh screen and mannitol (granular) (229.15 mg/wafer) was screened through a 12 mesh screen. Microcrystalline cellulose (60.0mg/wafer),

aspartame (6.0mg/wafer), flavours (5.2 mg/wafer), colloidal silicon dioxide (0.25 mg/wafer) and stearic acid (3.0 mg/wafer) was shaken together for 2 minutes. The colour and mannitol were blended and the above mixt. was added together with the coated acetaminophen particles then the mixt. was blended. The blend was compressed into wafers (400.0mg) on a rotary tablet press.
The above wafers were found to disintegrate in less than 30 seconds when placed on the tongue of a human. They did not leave a bitter aftertaste. (KKG)
PREFERRED MATERIALS
The compressible carbohydrate is mannitol, sorbitol, dextrose, sucrose, xylitol, lactose, or a mixt., thereof.
The coated particle comprises at least one pharmaceutical coated with a blend of a first polymer which is a cellulose acetate or cellulose acetate butyrate, and a second polymer which is polyvinyl pyrrolidone or hydroxypropyl cellulose.
The binder is cellulose, a cellulosic deriv., polyvinyl pyrrolidone, starch, modified starch or a mixt. thereof.
The pharmaceutical is acetaminophen (pref., ibuprofen (pref.), flurbiprofen, naproxen, aspirin (pref., pseudoephedrine, phenylpropanolamine, chlorpheniramine maleate, dextromethorphan, diphenhydramine, famotidine (pref.), loperamide (pref.), ranitidine, cimetidine, astemizole, terfenadine, terfenadine carboxylate, certirizine, a salt thereof or a mixt. thereof.
PREFERRED COMPOSITION
The dosage form has a hardness within the range of about 1.0 to 3.0 kp (pref. about 1.5 to 2.5 kp.)
The wt. ratio of the first polymer to the second polymer is within the range of about 90:10 to 50:50. The coated particle comprises about 5 to 60 wt.% of the blend of the first and second polymers. The wafer has a dia. of about 7/16 to about 3/4 inch and a thickness of about 0.05 to about 0.5 inch.
The wafer comprises:
coated particles (about 0.5 to 600 mg);
carbohydrate (about 250 to 750 mg.);
binder (about 20 to 100 mg);
and opt. additionally comprises:
a lubricant (about 4 to 60 mg.);
a colour (about 1 to 10 mg.);
a sweetener (about 1 to 10 mg.); and
a flavour (about 1 to 10 mg.).

L173 ANSWER 37 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1995-021210 [03] WPIX Full-text
ED 20050510
CR 1991-202078; 1996-019833
DNC C1995-009934 [03]

TI Prepn. of directly compressible naproxen compsn. - with good compressibility, and compactability and good flow characteristics

DC B05

IN CHOWHAN Z T; HAFEZZADEH H; KURAMOTO R; PENDLETON R O

PA (SYNT-C) SYNTEX PHARM INT LTD

CYC 1

PI US 5358717 A 19941025 (199503)* EN 6[0]
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ADT US 5358717 A Cont of US 1989-455109 19891222; US 5358717 A CIP of US 1991-759783 19910827; US 5358717 A US 1992-878145 19920504

PRAI US 1992-878145 19920504
US 1989-455109 19891222
US 1991-759783 19910827

IPCR A61K0031-185 [I,C]; A61K0031-19 [I,A]; A61K0009-14 [I,A]; A61K0009-14 [I,C]; A61K0009-16 [I,A]; A61K0009-16 [I,C]; A61K0009-20 [I,A]; A61K0009-20 [I,C]

EPC A61K0009-14; A61K0009-16H6B; A61K0009-16H6F; A61K0009-20H6F2; A61K0009-20P; A61K0031-19

AB US 5358717 A UPAB: 20050510

Prepn. of a directly compressible naproxen (I) compsn. comprises: (i) spray drying an aq. mixt. contg. 20-70% solid comprising 90.46-100% (I), opt. upto 6.25% binder and opt. up to 6.25% disintegrating agent, to obtain a spray dried (I) compsn. with free moisture content ≤ 1.63%; and (ii) combining this prod. with water and dry excipients to give a compsn. contg. 90-97% spray dried (I), 0.5-1.5% free moisture, 1-6% binder, 1-6% disintegrating agent and 0.1-2% lubricant. Step (i) is claimed per se.

USE - Naproxen, i.e d-2-(6'-methoxy-2-naphthyl)-propionic acid, is a well known antiinflammatory agent.

ADVANTAGE - The prods. are free flowing, have excellent compactibility and compressibility and are exceptionally suited for compression into tablets. The compsns. are stable and can be stored for a period of time prior to tabletting. Tablets prepd. from the compsn. possess good hardness, are stable and have good dissoln. characteristics. Due to the small amt. of excipients, the tablets are smaller and are more easily administered orally. The process gives an evenly blended mixt. from an aq. mixt. avoiding energy intensive drying and milling steps. ABDT US5358717

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WIDER DISCLOSURE

The method also relates to naproxen sodium. The disclosure also relates to the compsns. themselves.

EXAMPLES

35 kg (I) was combined with 1.4kg croscarmellose, 0.7kg povidone K-90 and 37.1kg water to give a soln. comprising 50% solids. The mixt. was spray dried through a schlick 2-fluid nozzle with 2mm dia. orifice. at 4 psig, main inlet temp. 239°C, fluid bed inlet temp. 88 °C and outlet temp. 66°C.

The spray dried compsn. was blended with magnesium stearate to produce a compsn. contg. 92% (I) USP, 1.6% free moisture, 4% croscarmellose sodium, NF, 2% povidone K-90, USP, and 0.2% magnesium stearate, NF.

The final blend had mean particle size 100-300µm, excellent flow through a hopper and was compressible on a rotary tablet press to 5 S.C. units under 600-800 lb load and compressible up to 10-18 S.C units under 5200 lb compression load. (AF)

PREFERRED PROCESS

The (I) in the aq. mixt. is obtd. directly from the final step in a synthesis of (I).

The disintegrating agent is croscarmellose sodium esp. used at 3-5%, the binder is hydroxypropylmethylcellulose or povidone (esp. used at 1-3%) and the compsn. contains 92-96% (I).

FS CPI

MC CPI: B04-C02A2; B04-C03B; B05-A01B; B10-C03; B10-C04E; B12-M11B; B12-M11G; B14-C03

CMC UPB 20050510
M2 *01* G021 G029 G221 H5 H541 H8 J0 J011 J1 J171 M210 M211 M272 M281 M312 M321 M331 M340 M342 M372 M391 M414 M510 M520 M531 M540 M630 M720 N104 N200 N513 N514 M903 M904
M6 *02* R112 R523 M903

AN 1982-85416E [40] WPIX Full-text
ED 20050420
TI Rotary press for twin layer tabletting
- has electro-magnet with return spring, driving slide with channel for dose removal in outer layer zone
DC B07; P71; X25
IN KRAVCHENKO V P; OLEINIK V A; SIRYACHENK A R
PA (ZHDA-R) ZHDANOV MEDICINE
CYC 1
PI SU 887263 B 19811207 (198240)* RU 4[4]
<--
ADT SU 887263 B SU 1980-2929267 19800523
IC IC B30B011-08
AB SU 887263 B UPAB: 20050420
The press comprises a rotor (1) with charging and pressing zones, and top and bottom plungers (3,4) in holes in dies (2), together with chargers (5,7). To increase productivity and quality, a device (9) is mounted between the charging zone and the outer-layer press zone, to remove a single dose of the material of this layer, made as a drive slide (10) with a removal channel. Preferably, the drive is an electromagnet (13) with a return spring. The tablets (18) are sampled via part (9) so that the vacuum channel matches the trajectory of motion of the dies. The vacuum system (20) and the control flap (17) also make up the assembly. Bul. 45/7.12.81.
FS CPI; GMPI; EPI
MC CPI: B11-C05; B12-M11
EPI: X25-A02
CMC UPB 20050420
M6 *01* Q010 Q435 R038 R112 R523 R528 R531 M903

L173 ANSWER 39 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1982-17665E [09] WPIX Full-text
ED 20050420
TI Rotary tabletting press - has conveying rotors each position fitted with horizontal and vertical tablets guiding plates and perforated stop
DC B07; P71
IN GOLDMAN Y A S; SHINDER E E
PA (GOLD-I) GOLDMAN YA S
CYC 1
PI SU 831629 B 19810525 (198209)* RU 5
<--
ADT SU 831629 B SU 1979-2771130 19790525
IC IC B30B011-12
AB SU 831629 B UPAB: 20050420
The rotary press for forming tablets from powder has horizontal and vertical plates fitted to each rotors position and a perforated

controller located concentrically to a rotor and above the dies, to increase products range. The dies (5) are fixed in a rotor's disc (4). A distributor (8) operates the cylinders pistons, each fitted with a bottom plunger (9). The top plungers are secured to the slider (11). The tablets are removed by means of air nozzles (12) supplied through the rotor (14) channels (15). The rotor has a concentric, perforated, stop (24). Each position of the conveying rotor (14) is fitted with horizontal and vertical plates (25,26). The powder in the die (5) is pressed by plunger (9,10) into a tablet. The plunger (10) is lifted (23) and lock (28) released from the piston rod (7). The plunger (9) goes up and pushes the table out of the die. The jets of air (12) blow the tablets off the plunger (9). The rotor (14) transfers them to the boxes. Bul. 19/23.5.81.

FS CPI; GMPI
MC CPI: B11-C05; B12-M04; B12-M11
CMC UPB 20050420
M6 *01* R038 R501 R523 R531 M903

L173 ANSWER 40 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1980-58785C [34] WPIX Full-text
ED 20050419
TI Rotary tabletting press air-blows powder from plunger surfaces - into shrouded chamber from which vacuum system extracts dust-laden air
AW PHARMACEUTICAL SWEET PEPPERMINT
DC B07; P33; P43; P71
IN WILLICH R
PA (FETT-N) FETTE GMBH WILHELM
CYC 8
PI BE 882654 A 19800731 (198034)* FR
<--
DE 2914201 A 19801016 (198043) DE
<--
GB 2046169 A 19801112 (198046) EN
<--
FR 2453016 A 19801204 (198105) FR
<--
US 4259049 A 19810331 (198116) EN
<--
DE 2914201 C 19821202 (198249) DE
<--
GB 2046169 B 19830511 (198319) EN
<--
CH 646097 A 19841115 (198451) DE
<--
AT 8001702 A 19841214 (198505) DE
<--

IT 1127002 B 19860521 (198740) IT
<--
PRAI DE 1979-2914201 19790407
IPCR B30B0011-02 [I,C]; B30B0011-08 [I,A]; B30B0015-00 [I,A]; B30B0015-00 [I,C]
EPC B30B0011-08; B30B0015-00M
NCL NCLM 425/073.000
NCLS 425/210.000; 425/353.000
AB BE 882654 A UPAB: 20050419
The plungers reciprocate to a approach each other closely inside a mould passage and so press a tablet. An air current is directed axially along each plunger surface. Part of each plunger is surrounded by a coaxial sleeve extending from the guide block. Fresh air is blown around the plunger and out towards the mould passage. Air from the sleeves is pref. discharged into an expansion chamber which shrouds the gap between guide block and mould wheel. The expansion chamber is connected to the suction of a vacuum system to carry away dust entrained in air extracted from the chamber.
Used in the mfg. of pharmaceutical tablets of compressed powder as well as sweets such as peppermints. The removal of powder dust from plungers prevents destructive grinding action between plunger and guide. Dust-laden air is collected in a vacuum system so that dust cannot pollute the atmos. of the factory.
FS CPI; GMPI
MC CPI: B11-C05; B12-M11
CMC UPB 20050419
M6 *01* R038 R112 R280 R523 M902

L173 ANSWER 41 OF 41 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1979-64725B [36] WPIX Full-text
ED 20050419
TI Tabletting press refrigerated to avoid overheating prod.
- has cooling for raw material to eliminate surface condensation
AW SUPPOSITORY
DC B07; P33; P71
IN ELTZSCHIG R; FRIEDRICHS K; STUBEN W
PA (FETT-N) FETTE GMBH WILHELM
CYC 7
PI BE 875659 A 19790816 (197936)* FR
<--
DE 2816974 A 19791025 (197944) DE
<--
GB 2025303 A 19800123 (198004) EN
<--
FR 2423327 A 19791221 (198006) FR
<--
US 4219320 A 19800826 (198037)# EN

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GB 2025303 B 19820506 (198218) EN
<--
CH 635778 A 19830429 (198320) DE
<--
IT 1116026 B 19860210 (198724) IT
<--
ADT US 4219320 A US 1979-43222 19790711
PRAI DE 1978-2816974 19780419
IC IC B30B011-08
IPCR B30B0015-00 [I,A]; B30B0015-00 [I,C]; B30B0015-30 [I,A]; B30B0015-30 [I,C]; B30B0015-34 [I,A]; B30B0015-34 [I,C]
EPC B30B0015-00B; B30B0015-30B; B30B0015-30B2; B30B0015-34
NCL NCLM 425/345.000
NCLS 425/259.000; 425/355.000
AB BE 875659 A UPAB: 20050419
A tabletting press has a horizontal, rotary table with die cavities which are charged by feed wheels from an edge hopper. Reciprocating rams compact material in the cavities. The press has a cooling system for the rotary table to prevent overheating of the compacted material. The cavity filling assembly is now fitted with a fluid refrigerant cooling circuit and air supplied to the pressing zone of the machine is also cooled. The fluid refrigerant cooling circuit pref. serves the wall of the filling hopper and/or the wall of the casing around the feed wheels. Used for compacting materials to form tablets, lozenges, etc. partic. materials which must not be overheated during pressing.
FS CPI; GMPI
MC CPI: B11-C05; B12-M08; B12-M11
CMC UPB 20050419
M1 *01* M417 M422 M423 M424 M740 M750 N100 N101 R031 R032 R033 R034 R036 R037 R038 R041 R042 R043 V300 V400 V406 V772 V780 V800 M902
M6 *02* R037 R038 R112 R523 R524 M902

=> D L174 1-28 TI

L174 ANSWER 1 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Rapid melt composition useful for delivery of prophylactic and therapeutic active materials to mammal e.g. psychotropic, comprises binder, salivating agent, diluent/bulking material, lubricant and a drug such as chondroitin, acetaminophen

L174 ANSWER 2 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

TI Pharmaceutical composition for sustained release of drugs, comprises preset amount of core comprising medicament and hydrophobic material as sustained release agent, and optionally contains lubricant, excipient and adjuvant polymer

L174 ANSWER 3 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Oral dosage form useful for treating e.g. diabetes mellitus, comprises 5-(4-(2-(N-methyl-N-(2-pyridyl)amino)ethoxy)benzyl)thiazolidine-2,4-dione in waxy mixture of glyceride-based material

L174 ANSWER 4 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Sustained release oral dosage form useful for the treatment of psychotic disorder e.g. schizophrenia, comprises ziprasidone and sustained release device for releasing portion of ziprasidone

L174 ANSWER 5 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Oral release formulation useful for the treatment of oral inflammation e.g. mucositis comprises L-glutamine and a solid or semi-solid edible medium that dissolves upon oral contact

L174 ANSWER 6 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Composition useful for treating acid related gastrointestinal disorders e.g. duodenal ulcer disease comprises acid labile proton pump inhibitor microencapsulated with material enhancing shelf-life of the composition, and antacid

L174 ANSWER 7 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Sustained release pharmaceutical composition in tablet form comprises a core comprising a medicament and a hydrophobic material, and excluding a polymer capable of swelling

L174 ANSWER 8 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Medicament granulate, especially useful in retarded release formulations containing corrosive and/or hydrophilic active agent, comprising mixture of active and retarding agents wetted with oil

L174 ANSWER 9 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Oral pulse dosage formulation useful for treating e.g. attention deficit disorder, narcolepsy and depression comprises methylphenidate formulated into first and second pulse dosage layers

L174 ANSWER 10 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Preparation of device useful for oral delivery of an agent involves the step of injection molding to apply an outer coating to

a core of the device

L174 ANSWER 11 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Sustained release composition in tablet form comprises medicament core with preset water solubility and hydrophobic material with preset melting point and excludes polymer disintegrant and water soluble low molecular excipient

L174 ANSWER 12 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Dosage form composition with improved mechanical strength comprises highly compressible ethylcellulose

L174 ANSWER 13 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Composition useful for coating solid dosage form of a medicament comprises a water insoluble polymer in the form of an aqueous latex dispersion and a water-soluble non-polymeric component

L174 ANSWER 14 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Molded articles, preferably soft capsules, are prepared by mixing a biopolymer with a liquid plasticizer whereby the moisture content of components is defined or controlled without a drying process

L174 ANSWER 15 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Composition for molded capsules, comprises preset amount of amino alkyl methacrylate copolymer, lubricant, dissolution modifying excipient, and optionally plasticizer and/or processing agent

L174 ANSWER 16 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Pharmaceutical composition for molded capsules, comprises preset amount of specific acrylate and methacrylates, lubricant, dissolution modifying excipient, and optionally surfactant, plasticizer or processing agent

L174 ANSWER 17 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Method useful for preparing tablets containing paroxetine hydrochloride anhydrate by a wet granulation process, drying the wet granules using a fluidized bed technique to obtain a specified water activity, followed by compression

L174 ANSWER 18 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Microcrystalline cellulose preparation for tableting, involves pressing, decompacting, cooking in pre-heated reactor, cooling partially depressurizing, filtering, bleaching and drying of pulp prepared by repulping

L174 ANSWER 19 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Pharmaceutical solution or solid oral dosage form comprising acid labile proton pump inhibitors (PPI) e.g. omeprazaole, useful for treating e.g. ulcer, contain buffering agent to prevent degradation of PPI in e.g. stomach

L174 ANSWER 20 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Composition useful in the treatment of migraine comprises paracetamol and niflumic acid

L174 ANSWER 21 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Controlled release dosage form comprises bi-layer core comprising drug- and a water-containing composition occupying separate regions and a water-permeable and a water-insoluble coating around the core with at least one delivery port

L174 ANSWER 22 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Bioactive agent tablet to disintegrate rapidly in body fluids, suitable for delivery to the oral, buccal, sublingual, vaginal, nasal, rectal and urethral cavities

L174 ANSWER 23 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Stable tablets which rapidly dissolve in the oral cavity, comprising drug, saccharide and amorphous saccharide

L174 ANSWER 24 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Oral dosage form used to deliver mucosal-irritating active agents to stomach - comprise active ingredient e.g. tetracycline antibiotic and is in oval form and is film coated

L174 ANSWER 25 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Solid dosage forms containing microcrystalline cellulose - used for delivery of agrochemicals, pharmaceuticals and veterinary products

L174 ANSWER 26 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Loading biologically active solute into crosslinked gel - in presence of loading polymer and pref. salt, to increase loading and stabilise active cpd., used e.g. in drug delivery

L174 ANSWER 27 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
TI Once-daily metronidazole dosage form - contg. (meth)acrylate copolymer and diluent(s), used for treating microbial infections, e.g. trichomoniasis

L174 ANSWER 28 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

TI Rotary tablet press - has hydrocylinder with journal bearings and punches operated by levers whose axles lie at a formula defined distance from the bearings

=> D L174 2,7,8,10,11,14,17,18,21,23,24,25,26,28 MAX

L174 ANSWER 2 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2006-635079 [66] WPIX Full-text
ED 20061013
CR 2003-532146
DNC C2006-195903 [66]
TI Pharmaceutical composition for sustained release of drugs, comprises preset amount of core comprising medicament and hydrophobic material as sustained release agent, and optionally contains lubricant, excipient and adjuvant polymer
DC B05; B07
IN MULYE N
PA (NOST-N) NOSTRUM PHARM INC
CYC 1
PI US 20060204573 A1 20060914 (200666)* EN 12[0]
ADT US 20060204573 A1 Provisional US 2001-297140P 20010608; US 20060204573 A1 Cont of US 2002-167368 20020610; US 20060204573 A1 US 2006-355346 20060216
FDT US 20060204573 A1 Cont of US 7052706 B
PRAI US 2006-355346 20060216
US 2001-297140P 20010608
US 2002-167368 20020610
IPCI A61K0009-22 [I,A]; A61K0009-22 [I,C]
IPCR A61K0009-20 [I,A]; A61K0009-20 [I,C]
EPC A61K0009-20H4; A61K0009-20H6B; A61K0009-20H6F; A61K0009-20H6F2
NCL NCLM 424/468.000
AB US 20060204573 A1 UPAB: 20061013
NOVELTY - A sustained release pharmaceutical composition in tablet form comprises a core comprising medicament (more than 25 wt.%) and hydrophobic material (3-20 wt.%) as sustained release agent. The composition optionally contains a lubricant, excipient and adjuvant polymer. The medicament has aqueous solubility of less than 1 g/10 ml of water at 25degreesC and 1 atmosphere, and more than 100 mg/liter of water at 25degreesC. The hydrophobic material has melting point of 40-100degreesC at 1 atmospheric pressure.

DETAILED DESCRIPTION - A sustained release pharmaceutical composition in tablet form comprises a core comprising medicament (more than 25 wt.%) and hydrophobic material (3-20 wt.%) as sustained

release agent. The composition optionally contains a lubricant, excipient and adjuvant polymer. The medicament has aqueous solubility of less than 1 g/10 ml of water at 25degreesC and 1 atmosphere, and more than 100 mg/liter of water at 25degreesC. The hydrophobic material has melting point of 40-100degreesC at 1 atmospheric pressure. The composition does not contain an ingredient in the core that causes disintegration of the tablet. The composition is prepared by blending the medicament, hydrophobic material, and optionally a lubricant, excipient and adjuvant polymer, at a temperature lower than the melting point of the hydrophobic material. The composition is formed in the absence of thermal infusion or melting the hydrophobic material, by utilizing shear mixture or by heating to temperatures below the melting point of hydrophobic material.

USE - As uncoated tablet (claimed) for sustained release of drugs such as antiinflammatory substance, stimulants, analgesics, vasodilators, cough suppressants, anabolic drugs, etc.

ADVANTAGE - The pharmaceutical composition enables sustained release of active ingredient, and improves patient compliance. The composition has favorable absorption and release property.

TECH ORGANIC CHEMISTRY - Preferred Components: The pharmaceutical composition further comprises a lubricant and excipient. The excipient is maltodextrin. The hydrophobic material is fatty acid or its salt, monoglyceride, diglyceride or triglyceride. The hydrophobic material is glyceryl behenate, hydrogenated vegetable oil, stearic acid, glyceryl monostearate, glyceryl palmito stearate or cetyl alcohol. The hydrophobic material is fatty acid having 10-30 carbons, its salt, fatty alcohol having 10-44 carbon atoms, or compound of formula (I).

R1=hydrogen or O=C-R4;

R2=is hydrogen or O=C-R5;

R3=hydrogen or O=C-R6;and

R4,R5,R6=lower alkyl or lower alkenyl having 9-29 carbon atoms;

Provided that: At least one of R1, R2 and R3 is group other than hydrogen.

PHARMACEUTICALS - Preferred Composition: The pharmaceutical composition contains hydrophobic material (5-15 wt.%, preferably 7-12 wt.%) and medicament (25-97 wt.%, preferably 40-85 wt.%). The medicament is theophylline or its salt, ferrous sulfate, clarithromycin or divalproex. The hydrophobic material is glyceryl behenate. The pharmaceutical composition contains water-soluble excipient (less than 20 weight/weight%).

Preferred Ratio: The weight ratio of the medicament with respect to the hydrophobic material is 9:1-5:4.

Preferred Properties: The melting point of the hydrophobic material is 40-90degreesC, preferably 55-75degreesC. The hydrophobic material has mean particle size of 10-200 microns, preferably 30-100 microns.

The excipient is insoluble in water.

ABEX EXAMPLE - Ferrous sulfate (160 mg), glyceryl behenate (30 mg) and maltodextrin (110 mg) were thoroughly mixed together in a V blended for 1 hour and compressed into tablet using rotary tablet press. The obtained tablet formulation had favorable drug release profile.

L174 ANSWER 7 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2004-662349 [64] WPIX Full-text
ED 20050531
DNC C2004-236532 [64]
TI Sustained release pharmaceutical composition in tablet form comprises a core comprising a medicament and a hydrophobic material, and excluding a polymer capable of swelling
DC B07
IN NIRMAL M; MULYE N
PA (NOST-N) NOSTRUM PHARM INC
CYC 100
PI WO 2004078164 A1 20040916 (200464)* EN 74[0]
AU 2003225649 A1 20040928 (200502) EN
EP 1599189 A1 20051130 (200578) EN
BR 2003018167 A 20060221 (200617) PT
MX 2005009469 A1 20051201 (200628) ES
JP 2006514672 W 20060511 (200635) JA 25
NZ 542176 A 20071221 (200819) EN
ADT WO 2004078164 A1 WO 2003-US6505 20030304; AU 2003225649 A1 AU 2003-225649 20030304; BR 2003018167 A BR 2003-18167 20030304; EP 1599189 A1 EP 2003-816186 20030304; AU 2003225649 A1 WO 2003-US6505 20030304; EP 1599189 A1 WO 2003-US6505 20030304; BR 2003018167 A WO 2003-US6505 20030304; MX 2005009469 A1 WO 2003-US6505 20030304; JP 2006514672 W WO 2003-US6505 20030304; JP 2006514672 W JP 2004-569167 20030304; MX 2005009469 A1 MX 2005-9469 20050905; NZ 542176 A NZ 2003-542176 20030304; NZ 542176 A WO 2003-US6505 20030304
FDT AU 2003225649 A1 Based on WO 2004078164 A; EP 1599189 A1 Based on WO 2004078164 A; BR 2003018167 A Based on WO 2004078164 A; MX 2005009469 A1 Based on WO 2004078164 A; JP 2006514672 W Based on WO 2004078164 A; NZ 542176 A Based on WO 2004078164 A
PRAI WO 2003-US6505 20030304
IC ICM A61K009-22
IPCI A61K0031-519 [I,C]; A61K0031-522 [I,A]; A61K0031-7042 [I,C]; A61K0031-7048 [I,A]; A61K0033-26 [I,A]; A61K0047-10 [I,A]; A61K0047-12 [I,A]; A61K0047-14 [I,A]; A61K0047-36 [I,A]; A61K0047-44 [I,A]; A61K0009-22 [I,A]

IPCR A61K0009-20 [I,A]; A61K0009-20 [I,C]; A61K0009-22 [I,A]; A61K0009-22 [I,C]
EPC A61K0009-20H4
ICO K61K0009:20H6F4; K61K0009:20P
AB WO 2004078164 A1 UPAB: 20060203
NOVELTY - Sustained release pharmaceutical composition (I) in tablet form comprises a core comprising a medicament (A) and a hydrophobic material (B) as the sustained release agent and excluding a polymer (C) capable of swelling that causes disintegration of the tablet and high concentration of water soluble low molecular weight excipient.
DETAILED DESCRIPTION - Sustained release pharmaceutical composition (I) in tablet form comprises a core comprising a medicament (A) and a hydrophobic material (B) as the sustained release agent and excluding a polymer (C) capable of swelling that causes disintegration of the tablet and high concentration of water soluble low molecular weight excipient, the (A) being present in an amount greater than about 25% of (I) and having a water solubility less than about 1 g/10 ml of water at 25degreesC and 1 atm, and more than about 100 mg/1 l of water at 25degreesC and 1 atm, (B) having a melting point least about 40-100degreesC at 1 atm pressure, and being present in an amount ranging from about 3-less than about 20%wt. of (I) and in an amount by weight less than that of (A).
An INDEPENDENT CLAIM is also included for preparation of (I).
USE - The composition is useful for sustained release of medicament (claimed).
ADVANTAGE - Preparation of (I) is simple, economical, incorporates significantly less hydrophobic material and avoids the expense associated with the high shear mixer.
TECH ORGANIC CHEMISTRY - Preparation (claimed): Preparation of (I) (oral dosage form) comprises blending (A) and (B) and optionally a lubricant, an excipient and an adjuvant polymer to form a substantially homogenous and uniform blend, the mixture excluding a polymer capable of swelling that causes disintegration of the tablet and high concentration of low molecular weight excipient, the medicament being present in an amount greater than about 25%wt of (I) and having a water solubility less than about 1 g/10 ml of water at 25degreesC and 1 atm, and greater than about 100 mg/l of water at 25degreesC and 1 atm, (B) having a melting point ranging from at least about 40-100degreesC at 1 atm pressure, and being present in an amount ranging from about 3-20%wt. of (I), and in an amount by weight less than that of (A); and compressing the product thus obtained to form a tablet, the (I) being formed in the absence of melting the (B) or utilizing a high shear mixer or by heating to temperatures slightly below the melting point of the hydrophobic material.
Preferred Process: (A), (B) and optionally an excipient and an adjuvant are mixed together to form a substantially homogenous and

uniform first blend, and a lubricant in lubricating effective amounts is added to the first blend and is mixed therewith to form a substantially uniform and homogenous second blend, where the second blend is compressed to form a tablet.

PHARMACEUTICALS - Preferred Composition: The tablet is uncoated. (B) is present in an amount ranging from about 5-15 (preferably 7-12) %wt. of (I). The weight ratio of the medicament to hydrophobic material ranges from about 9:1 -about 5:4. The melting point of (B) is 40-90degreesC (preferably 55-75degreesC). (B) has a mean particle size ranging from about 10-200 (preferably 30 -100) microns. (A) is present in an amount ranging from about 25-97 (preferably 40-85)%wt. of (I). (I) further comprises a lubricant , excipient (maltodextrin).(B) is a fatty acid or its salt or a monoglyceride, diglyceride or triglyceride (preferably glyceryl behenate). The fatty acid is 10-30C fatty acid, 10-44C fatty alcohol or CH2-OR1-CH-OR2-CH-OR3

R1 = C(O)R4 or H

R2 = H or C(O)R5

R3 = H or C(O)R6

R4, R5 and R6 = lower alkyl or 9-29C lower alkenyl

where at least one of R1, R2 and R3 is other than hydrogen). (A) is theophylline or its salt, ferrous sulfate, clarithromycin or divalproex.

ABEX ADMINISTRATION - Administration of (I) is oral (claimed). No dosage given.

EXAMPLE - Ferrous sulfate (160 mg), glyceryl behenate (30 mg) and maltodextrin (I IO mg) were thoroughly mixed together in a blender for one hour and compressed into a tablet using a rotary tablet press. The dissolution was determined using USP apparatus I in water

L174 ANSWER 8 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 2004-534843 [52] WPIX

ED 20050530

DNC C2004-196912 [52]

TI Medicament granulate, especially useful in retarded release formulations containing corrosive and/or hydrophilic active agent, comprising mixture of active and retarding agents wetted with oil

DC B07

IN KLOKKERS K; MEYER H E E; OTTO I E

PA (HEXA-N) HEXAL AG

CYC 105

AB DE 10300325 A1 UPAB: 20060121

NOVELTY - Production of a granulate for medicament formulations involves wetting a mixture consisting of (or containing) active agent(s) and retarding agent(s) with an oil, then granulating the

mixture. Alternatively the process involves mixing the active agent(s) and retarding agent(s), wetting the mixture with the oil and granulating.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(1) the production of tablets, by processing a granulate obtained as above to form tablets;

(2) granulates and tablets obtained by the processes; and

(3) granulate for medicament formulations, consisting of or containing a mixture of active agent(s) and retarding agent(s) wetted with an oil.

USE - The process is especially used for producing retarded and sustained release formulations containing corrosive and/or hydrophilic active agent(s), such as tilidine hydrochloride (which is strongly hygroscopic and reacts with metal surfaces such as tableting punches). Other corrosive active agents include ranitidine hydrochloride, clindamycin hydrochloride, doxepin hydrochloride, citalopram hydrobromide, amitriptyline, cetrizine, piroxicam and naxolone hydrochloride.

ADVANTAGE - A simple and effective process is provided for producing retarded release formulations having a defined release profile. The oil wets the surface of the active agent particles and forms a hydrophobic protective film, so that corrosive and/or hydrophilic active agents can be processed without the need for special climatized working environments and corrosion-resistant apparatus. The granules are non-sticky and readily processed, e.g. by sieving and tableting. The oil minimizes direct contact between the active agent and apparatus surfaces, so that corrosion of the apparatus and contamination of the active agents with metal ions are minimized.

TECH PHARMACEUTICALS - Preferred Process: The mixtures of active agent(s) and retarding agent(s) optionally contain one or more auxiliaries, specifically fillers, flow regulators, wetting agents and/or disintegrating agents. The oil is applied by spraying, preferably at room temperature; and is specifically a natural or synthetic oil, a solution of wax in oil or a mobile liquid wax, preferably forming 0.2-20 (especially 1-7.5) wt. % of the granulate. The active agents are corrosive and/or hydrophilic; and are contained in the granulate at 0.1-98 (preferably 0.5-70) wt. %. The retarding agents are lipophilic, and preferably used in combination with a hydrogel matrix and/or a structure matrix former (the matrix former optionally being used together with water-soluble auxiliaries). The granules optionally include an outer phase consisting of retarding agent(s). Granulation is carried out in a fluidized bed granulator or a ploughshare mixer, preferably in presence of a granule binder (especially in solution form). The granules are optionally processed to give tablets, specifically in presence of auxiliaries (preferably fillers, flow regulators,

wetting agents and/or disintegrating agents), the tablets optionally being provided with a coating.

ABEX EXAMPLE - Tablets each contained 102.87 mg tilidine hydrochloride hemihydrate, 8.80 mg naxolone hydrochloride, 40.00 mg hydroxypropyl methyl cellulose, 2.00 mg Aerosil (RTM), 68.50 mg hydrogenated castor oil, 64.89 mg Compritol (RTM), 7.50 mg Kollidon (RTM), 19.11 mg neutral oil, 150 mg purifed water, 66.38 mg Tablettose (RTM) and 2.0 mg magnesium stearate. The tablets were prepared by weighing out and screening tilidine hydrochloride hemihydrate, naxolone hydrochloride, hydroxypropyl methyl cellulose, Aerosil (RTM), hydrogenated castor oil and Compritol (RTM); mixing in a fluidized bed granulator; spraying the mixture in the granulator with neutral oil followed by a solution of Kollidon (RTM) in water; drying the granules in the granulator; screening the granules through a 1 mm sieve; mixing the obtained free-flowing granulate with Tablettose (RTM) and magnesium stearate in a free-fall mixer; and pressing to give 382 mg tablets.

L174 ANSWER 10 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2003-568884 [53] WPIX
ED 20050531
DNC C2003-153302 [53]
TI Preparation of device useful for oral delivery of an agent involves the step of injection molding to apply an outer coating to a core of the device
DC A32; A96; B07
IN CLARKE A J; CLARKE A J G; GLINECKE R; GLINECKE R G; LI C L; LI C L G; MARTINI L G; MARTINI L G G
PA (CLAR-I) CLARKE A J; (GLIN-I) GLINECKE R; (LICL-I) LI C L; (MART-I) MARTINI L G; (SMIK-C) SMITHKLINE BEECHAM PLC
CYC 100
AB WO 2003020246 A1 UPAB: 20060120
NOVELTY - Preparation of a device comprising a core including an agent covered by an outer coating, involves applying the outer coating by injection molding the coating around the core. The outer coating includes at least one opening communicating from the exterior of the device to the core.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a die or mold having a cavity in which the tablet core may be located with a space around the core to define the required shape and dimensions of the coating with at least one internal member extending from the interior surface of the mold cavity to about the core and to define the shape and position of at least one opening; and

(2) a device including the core having the agent covered by the outer coating. The coating includes at least one opening communicating from the exterior of the device to the core.

USE - For producing device, which is useful for oral delivery of the agent (claimed), for immediate, delayed or sustained release e.g. to achieve release of the agent at a pre-determined part of the gastro-intestinal tract.

ADVANTAGE - The process is more robust and simpler to operate than conventional methods. The coating is applied to create the device in a single operation i.e. no further processing of the coating is required such as mechanical drilling of the coat to expose the core, which permits an improved method of producing devices with a varying number, size and shape of openings.

TECH INSTRUMENTATION AND TESTING - Preferred Process: Preparation of the device involves:

(1) providing a core of the device comprising the agent;
(2) locating the core within the mold cavity surrounding the core. The mold cavity defines the required dimensions of the outer coating; and also the required position, shape and dimensions of at least one opening;
(3) injecting a fluid moldable material into the cavity;
(4) allowing the material to set to form the coating; and
(5) separating the formed device from the cavity.

The molding pressure is less than 400 - 450 kg/cm2.

Preferred Components: At least one internal member of the mold cavity is resiliently mounted so as to be able to move reciprocally resiliently inward and outward relative to the mold cavity or to apply a resilient pressure of 14 kg/cm2 to the tablet core or to be resiliently moveable under the applied pressure. The internal member is provided with a vacuum conduit passing through it to the outside of the mold, such that the reduced pressure may be applied to a tablet core in contact with the member to assist in retaining the core in place in the mold. The die or mold closes along a horizontal axis.

Preferred Device: The coating is a polymeric material exhibiting a melt flow index of 15 - 30 g/10 minutes, applied by injection molding the coating around the core. The coating has a thickness of 0.1 - 2.0 mm. The material of the coating blocks exposure of the core to an environmental fluid. The core has a cylindrical shape having two opposite facing generally convex circular end faces; or a convex or a bi-convex shape comprising two opposite-facing domed surfaces which are generally circular or elliptical in plan. The core conforms to the outer shape of the core and the coating has two opposite facing openings. The core has a seating indentation of a shape corresponding to the part of the internal member of the mold that contacts the core, and so

positioned on the core that when the mold encloses the tablet core the member seats in the indentation. The core has at least one seating projection to engage with the mold cavity.

POLYMERS - Preferred Component: The polymeric material is polymethacrylate copolymers, natural wax and lipid, biodegradable polymer in general, polyvinyl acetate, cellulose acetate, butyrate and phthalate, ethylene vinyl acetate, hydroxypropyl cellulose, copolymer of methacrylic acid, methylmethacrylate, methyl acrylate or silicone.

ABEX EXAMPLE - The following tablet core was formed by mixing together the active ingredients with excipients and compressed to form the tablet core. Tablet core consisted of active ingredient (10 %), microcrystalline cellulose (60 %), lactose (24 %), starch glycolate (disintegrant) (5 %) and magnesium stearate (lubricant) (1 %). The coating material used was a low density polyethylene (LD600BA natural). This material demonstrated a wide range of processing temperatures (160 - 240 degrees C) and had a melt flow index of 20.5 g/10 minutes. Operating conditions utilized were 150 degrees C and pressure of 400 psi. The injection molding machine was used. The tablet core had a diameter of 8 mm. The coating had a thickness, as defined by the gap in the cavity between the core and the inner wall of the cavity of ca. 0.5 mm. It has been found that these injection molding operating conditions did not have an adverse effect on the tablet core i.e. mechanical integrity was maintained.

L174 ANSWER 11 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2003-532146 [50] WPIX Full-text
ED 20050531
CR 2006-635079
DNC C2003-143608 [50]
TI Sustained release composition in tablet form comprises medicament core with preset water solubility and hydrophobic material with preset melting point and excludes polymer disintegrant and water soluble low molecular excipient
DC B05; B07
IN MULVE N; MULYE N
PA (NOST-N) NOSTRUM PHARM INC
CYC 1
PI US 20030077324 A1 20030424 (200350)* EN 12[0]
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US 7052706 B2 20060530 (200636) EN
ADT US 20030077324 A1 Provisional US 2001-297140P 20010608; US 20030077324 A1 US 2002-167368 20020610
PRAI US 2002-167368 20020610
US 2001-297140P 20010608

IPCI A61K0006-00 [I,A]; A61K0006-00 [I,C]
IPCR A61K0009-20 [I,A]; A61K0009-20 [I,C]; A61K0009-22 [I,A]; A61K0009-22 [I,C]
EPC A61K0009-20H4; A61K0009-20H6B; A61K0009-20H6F; A61K0009-20H6F2
NCL NCLM 424/401.000
AB US 20030077324 A1 UPAB: 20050531

NOVELTY - Sustained release composition in tablet form comprises more than 25 wt.% of medicament core and 3-20 wt.% of hydrophobic material and excludes a polymer (disintegrating agent) capable of swelling and water-soluble low molecular excipient. The medicament has water solubility of less than 1 g/10 mL to more than 100 mg/L of water at 25 degrees C and 1 atm.

DETAILED DESCRIPTION - A sustained release pharmaceutical composition in tablet form comprises a core comprising more than 25 weight% (wt.%) of medicament and 3-20 wt.% hydrophobic material having melting point of 40-100 degrees C at 1 atm pressure as the sustained release agent and excluding a polymer capable of swelling that causes disintegration of the tablet and high concentration of water-soluble low molecular weight excipient. The medicament has water solubility of less than 1 g/10 mL to more than 100 mg/L of water at 25 degrees C and 1 atm.

An INDEPENDENT CLAIM is included for the preparation of sustained release composition in oral form by blending medicament and hydrophobic material and optionally a lubricant, excipient and adjuvant polymer to form a substantially homogenous and uniform blend, and compressing into tablets. The composition is formed by melting in the absence of hydrophobic material, utilizing a high shear mixer or by heating to temperature slightly below the melting point of the hydrophobic material.

USE - The composition is used as a sustained release pharmaceutical composition in tablet form (claimed).

ADVANTAGE - The controlled release dosage forms can be manufactured by incorporating significantly less hydrophobic material using simple manufacturing process such as direct compression, which involves compression of the various ingredients after a simple mixing procedure. The obtained composition has excellent sustained release property and avoids hazards associated with the use of toxic or flammable solvents used in wet granulation methods. The drawbacks of formulating with hydrophobic material, e.g. waxes, such as dimensional stability, with respect to heat and abrasion are eliminated. The technique minimizes the heat and energy in the manufacture of unit dosage forms. Solid dry forms such as tablets, prepared by the method are hard and dense, have low friability and provide control and sustained release over an extended period. Solid dry forms are stable and their release rate does not change to any significant extent over an extended period of storage.

TECH PHARMACEUTICALS - Preferred Composition: The tablet is

uncoated. The composition contains 5-15 (7-12) weight% (wt.%) of a hydrophobic material and 25-97 (40-85) wt.% of medicaments . The weight ratio of the medicament to hydrophobic material is 9:1-5:4.
Preferred Properties: The hydrophobic material has a melting point of 40-90 (preferably 55-75)degreesC and a mean particle size of 10-200 (preferably 30-100) microns.
Preferred Components: The composition further contains a lubricant and excipient (maltodextrin). The hydrophobic material is a fatty acid, its salt, monoglyceride, diglyceride or triglyceride. It is a 10-30C fatty acid or its salt, 10-44C fatty alcohol or a fatty acid of formula (I).
R1 = H or O=C-R4;
R2 = H or O=C-R5;
R3 = H or O=C-R6; and
R4, R5, R6 = lower 9-22C alkyl or alkenyl.
Provided that at least one of R1,R2 and R3 is other than H.
Preferred Medicament: The medicament is theophylline or its salt, ferrous sulfate, clarithromycin or divalproex.
Preferred Process: The medicament, hydrophobic material and optionally an excipient and adjuvant are mixed together to form a substantially homogenous and uniform first blend, and a lubricant is added to the first blend and is mixed to form a substantially uniform and homogenous second blend. The second blend is compressed to form a tablet.

ABEX SPECIFIC COMPOUNDS - Use of 6 hydrophobic materials is specifically claimed, i.e. glyceryl behenate, hydrogenated vegetable oil, stearic acid, glyceryl monostearate, glycerylpalmito stearate or cetyl alcohol.
EXAMPLE - 160 mg of ferrous sulfate, 30 mg of glyceryl behenate and 110 mg of maltodextrin were thoroughly mixed together in a V blender for one hour and compressed into a tablet using a rotary tablet press. Dissolution rate of the tablet was determined using USP apparatus I in water. The tablet showed 36 weight/weight% (w/w%), 58 w/w%, 72 w/w% and 82 w/w% drug release after 1, 2, 3 and 4 hours, respectively.

L174 ANSWER 14 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2003-177271 [18] WPIX Full-text
ED 20050528
DNC C2003-046797 [18]
TI Molded articles, preferably soft capsules, are prepared by mixing a biopolymer with a liquid plasticizer whereby the moisture content of components is defined or controlled without a drying process
DC A11; A31; A96; B07

IN BROCKER E; ENGEL D W; MENARD R
PA (SWCA-N) SWISS CAPS RECHTE & LIZENZEN AG
CYC 26
PI EP 1258242 A1 20021120 (200318)* DE 20[6]
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ADT EP 1258242 A1 EP 2001-111739 20010515
PRAI EP 2001-111739 20010515
IPCR A61J0003-07 [I,A]; A61J0003-07 [I,C]; A61K0009-48 [I,A]; A61K0009-48 [I,C]
EPC A61J0003-07; A61K0009-48B; A61K0009-48Z
AB EP 1258242 A1 UPAB: 20050528
NOVELTY - Molded articles, preferably soft capsules, are prepared by:

(A) mixing a plant derived biopolymer with a liquid plasticizer to form a homogeneous raw material mixture; and

(B) melting raw material and forming a film and molded articles.

The moisture content of all components in the process from the raw material mixture to the finished molded article is defined or controlled without a drying process.

DETAILED DESCRIPTION - Molded articles, preferably soft capsules, are prepared by:

(A) mixing at least a first plant derived biopolymer in powder or granulate form with at least one liquid plasticizer, preferably in the form of a syrup, optionally together with additives to form a homogeneous raw material mixture;

(B) melting the mixture by heating under elevated pressure in a processing device, preferably in an extruder to form a thermoplastically processable composition (C) optionally preparing an intermediate product, preferably a granulate following cooling of the composition from (B) with renewed processing to form a thermoplastically processable composition;

(C) forming at least one film from the composition prepared in step (B); or

(D) producing molded articles using the film in an intermittent or continuous process at a forming station, preferably a rotary-die encapsulating machine.

The moisture content of all components in the overall process from the raw material mixture to the finished molded article is defined or controlled such that the finished molded article leaving the forming station has the required residual moisture content corresponding to the conditions of storage and/or use without a drying process.

USE - The molded articles are useful as soft capsules for the packaging of medicines and food supplements.

ADVANTAGE - The molded articles do not contain gelatine and have good storage properties for at least one year.

DESCRIPTION OF DRAWINGS - The drawing is a cross-sectional schematic view of a twin screw extruder showing the temperature profile.

TECH POLYMERS - Preferred Components: The first plant derived biopolymer is starch or modified starch in native and/or crystalline, non-destructured form.

The raw material mixture comprises a second biopolymer, preferably starch, modified starch, cellulose, preferably partially hydroxypropylated cellulose, alginate, pectin, agar, carrageenan, galactomannan, xanthan gum, tamarind, tragant gum, karaya gum, chitosan, glucomannan, casein, dextrin, cyclodextrin, pullulan or arabinogalactan.

The first and second biopolymer have a moisture content of 10-30 (preferably 15-23)%.

The plasticizer is glycerine, a syrup of hydrogenated, partially hydrolyzed starch, decomposition products containing oligosaccharides and monosaccharides, sorbitol, malitol, mannitol, erythritol, xylitol and/or traces of reduced sugar. The plasticizer is in the form of a polysyrup having a water content of 15-30%. At least 1 wt.% more of a hydrolyzed and hydrogenated starch originating polyol is present than other plasticizers.

The surface of the molded article is coated with a lipophilic or wax containing sealing substance to reduce moisture uptake or loss, preferably beeswax (E90), carnauba wax (E903), candellila wax (E902), berry wax, montanglycol wax (E912), polyethylene glycol wax oxidate (E914), shellac (E904), mono-, di- and triglycerides of edible fatty acids (E471), sugar esters of edible fatty acids (E476) and dimetzylpolysiloxanes (E900).

Preferred Process: The raw material mixture is melted at 80-160 degreesC at a pressure that at least corresponds to the vapor pressure at that temperature, whereby water vapor allowed to leave the processing device via a decompression zone or water is injected into the processing device via an injection zone. The film is formed by extrusion at 50 atmospheres and 80-105 degreesC via a slit nozzle into an atmospheric environment. The film is 0.2-2 mm thick and has a Staudinger index value of at lest 40 (50), preferably at least 80 ml/g.

ABEX EXAMPLE - A composition (initial water content 23.8%) comprising hydroxypropylated potato starch (60.2 parts) (21% moisture content, 0.1 mol.% hydroxypropyl group content), sorbitol syrup (37.5 parts) (70% dry mass), liquid lecithin (1.1 parts) and glycerine monostearate (1.2 parts) was processed through a twin screw extruder. - The water content of the processed composition (25 degreesC, 60% relative humidity) was 11.5 %.

AN 2002-723228 [78] WPIX

ED 20050527
DNC C2002-204717 [78]
TI Method useful for preparing tablets containing paroxetine hydrochloride anhydrate by a wet granulation process, drying the wet granules using a fluidized bed technique to obtain a specified water activity, followed by compression
DC A96; B02
IN FELUMB N C; HENRIKSEN K L; PEDERSEN S B; FELUMB C; HENRIKSEN L; PEDERSEN B
PA (FELU-I) FELUMB N C; (GEAA-C) GEA FARMACEUTISK FABRIK AS; (HENR-I) HENRIKSEN K L; (PEDE-I) PEDERSEN S B
CYC 96
AB WO 2002069969 A1 UPAB: 20060120
NOVELTY - Manufacture of pharmaceutical tablets containing paroxetine hydrochloride anhydrate involves a wet granulation process in which an aqueous granulation liquid was added to a mixture of the anhydrate and excipients under high-shear conditions, and drying the wet granules using a fluidized bed technique to obtain a water activity within a specified range, followed by compressing the dried granules.

DETAILED DESCRIPTION - Manufacture of pharmaceutical tablets containing paroxetine hydrochloride anhydrate (a) involves subjecting crystalline (a) together with adjuvants comprising filler, disintegrant, binder, and water to a high-shear mixing operation by

(a) Continuing the mixing to granulate the resulting mixture;

(b) Fluidizing the resulting granulate in a flow of heated drying air to dry the granulate;

(c) Continuing the drying until the moisture content of the granulate has been reduced to such an extent that the water activity of the granulate is 0.10 - 0.25 aw, when measured;

(d) Optionally adding at least one adjuvant;

(e) Mixing a glidant into this granulate and compressing the resulting mixture into tablets each having a pre-determined content of (a).

ACTIVITY - Antidepressant; Tranquilizer.

MECHANISM OF ACTION - None given.

USE - For manufacture of pharmaceutical tablets containing paroxetine hydrochloride anhydrate, which is useful in the treatment and prophylaxis of depression, anxiety and several other disorders.

ADVANTAGE - The method forms the stable tablets without conversion of the anhydrate into hemihydrate and provides very fast drying of the granules. The tablets produced show no tendency of discoloration during storing. Tablets produced by the process have been stored for several months after which no detectable conversion of the crystalline paroxetine hydrochloride anhydrate had occurred. No hemihydrate was found and no conversion into other crystalline

forms than the one of the starting material was detected. Also the mechanical stability of the tablet is satisfactory.

TECH PHARMACEUTICALS - Preferred Method: At least a part of the binder and at least a part of the water is added as an aqueous binder solution to a mixture of paroxetine anhydrate chloride, the filler and disintegrant while the mixture is subjected to high-shear mixing. The granulate is dried to a water activity of 0.15 and 0.22 aw. The crystalline (a), mannitol, microcrystalline cellulose and sodium starch glycolate are subjected to high-shear mixing and simultaneously an aqueous solution of copovidone is added slowly to obtain the desired granulation. The aqueous solution and optionally further water, are added in such an amount that a moisture content in the granulated mixture of 10 - 30 wt.% is obtained. The tablets formed by the compressing are subjected to a coating operation using an aqueous coating liquid.

Preferred Components: The each tablet produced has a weight of 100 - 750 mg and each contains 10 - 60 mg paroxetine, calculated as the free base.

POLYMERS - Preferred Components: The filler comprises at least one of microcrystalline cellulose, mannitol, calcium phosphates, lactose, starch, sorbitol, and succhrose. The disintegrant comprises at least one of sodium starch glycolate, starch, gelatinated starch, crospovidone or micro crystalline cellulose. The binder comprises at least one of polyvinyl pyrrolidone, gelatine, starch, methyl cellulose, hydroxypropylcellulose and copovidone.

ABEX ADMINISTRATION - The composition is administered orally.

EXAMPLE - Crystalline paroxetine hydrochloride anhydrate (22.22 kg), PH101 (microcrystalline cellulose) (a) (80 kg), sodium starch glycolate (6 kg) and mannitol (72 kg) were introduced. After mixing in dry condition, an aqueous solution of Kolidon VA64 (copovidone) (8 kg) in water (48 kg) was added slowly and the high-shear mixing continued to finish the granulation process. The wet granulate was immediately transferred to a fluidized bed dryer and dried to a water activity of approximately 0.20 aw after 1 hour, followed by subsequent sieving the granules and transferred into a cone blender and mixed with (a) (47.7 kg), anhydrous colloidal silica (0.48 kg) and sodium stearyl fumarate (3.6 kg). The resulting dry mixture and the further adjuvants were compressed into tablets using a conventional rotary press. A total of 240 kg tablets corresponding to 1 mio. pieces were produced, each comprising the same amount of crystalline paroxetine hydrochloride anhydrate, corresponding to 20 mg of the paroxetine base. The tablets were film-coated using a coated liquid containing methylhydroxypropyl cellulose (1.382 kg), micronized talc (0.806 kg), titanium dioxide (0.288 kg) and purified water (26.324 kg). The tablets thus produced were subjected to several tests. Stability studies of tablets packed in Al/PVC blister cards

or polyethylene containers was performed with satisfactory results. Also breakability studies were performed. Comparative dissolution test was performed. The results showed that more than 80% of the paroxetine was released from the film coated tablets within 10 minutes. XRD studies was performed on the finished product to confirm that no conversion of the crystalline paroxetine hydrochloride anhydrate to hemihydrate form takes place during manufacture and storage. It was also observed that the tablets, whether coated or not, did not show any discoloration even after prolonged storage.

L174 ANSWER 18 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 2002-394744 [42] WPIX Full-text
ED 20050526
CR 2002-599297; 2003-182240
DNC C2002-111223 [42]
TI Microcrystalline cellulose preparation for tableting, involves pressing, decompacting, cooking in pre-heated reactor, cooling partially depressurizing, filtering, bleaching and drying of pulp prepared by repulping
DC F09
IN CHORNET E; CLOUTIER S; JOLLEZ P
PA (KEME-N) KEMESTRIE INC
CYC 96
PI WO 2002036877 A1 20020510 (200242)* EN 30[3]
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AU 2002020388 A 20020515 (200258) EN
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EP 1332255 A1 20030806 (200353) EN
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BR 2001015148 A 20040720 (200451) PT
ADT WO 2002036877 A1 WO 2001-CA1550 20011102; BR 2001015148 A BR 2001-15148 20011102; EP 1332255 A1 EP 2001-992812 20011102; EP 1332255 A1 WO 2001-CA1550 20011102; BR 2001015148 A WO 2001-CA1550 20011102; AU 2002020388 A AU 2002-20388 20011102
FDT AU 2002020388 A Based on WO 2002036877 A; EP 1332255 A1 Based on WO 2002036877 A; BR 2001015148 A Based on WO 2002036877 A
PRAI US 2000-245148P 20001103
IPCR D21C0009-00 [I,A]; D21C0009-00 [I,C]
EPC D21C0009-00B
AB WO 2002036877 A1 UPAB: 20050526
NOVELTY - A pulp prepared by repulping is pressed decompacted and fed into a pre-heated reactor. The pre-heated reactor cooks the pulp at a temperature, time and pressure selected to obtain pulp having desired degree of polymerization. The reactor is cooled and partially depressurized by injecting water into the reactor. The obtained pulp

is filtered, bleached and dried to prepare microcrystalline cellulose.

USE - For preparing microcrystalline cellulose used for tableting, cream used in pharmaceuticals and cosmetics, fat replacer, chromatography support and complexation with transition metals for enzyme immobilization.

ADVANTAGE - The microcrystalline cellulose has fibrous appearance, and integrity, and does not necessitate use of mineral acids, sulfur dioxide or carbon dioxide. The microcrystalline cellulose is produced in absence of violent non-selective pressurization. A controlled depressurization, limits production of un-desirable derivatives and allows high yield of microcrystalline cellulose. Filtration of treated product is carried out at faster rate. The final product has higher degree of brightness. The process for preparing microcrystalline cellulose is carried out in a low acidic environment, which does not cause massive depolymerization.

FS CPI

MC CPI: F05-A02A; F05-A02B

L174 ANSWER 21 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

AN 2001-529564 [58] WPIX

ED 20050526

DNC C2001-157919 [58]

TI Controlled release dosage form comprises bi-layer core comprising drug- and a water-containing composition occupying separate regions and a water-permeable and a water-insoluble coating around the core with at least one delivery port

DC A96; B07

IN APPEL L E; BEYERINCK R A; CHIDLAW M B; CURATOLO W J; FRIENSEN D T; FRIESEN D T; GOVIND A; SMITH K L; THOMBRE A G; APPEL L; BEYERINCK R; CHIDLAW M; CURATOLO W; FRIESEN D; SMITH K; THOMBRE A

PA (PFIZ-C) PFIZER PROD INC; (APPE-I) APPEL L E; (BEYE-I) BEYERINCK R A; (CHID-I) CHIDLAW M B; (CURA-I) CURATOLO W J; (FRIE-I) FRIESEN D T; (SMIT-I) SMITH K L; (THOM-I) THOMBRE A G; (PFIZ-C) PFIZER INC

CYC 93

AB WO 2001047500 A1 UPAB: 20060117

NOVELTY - A controlled release dosage form comprises a core (a) and a coating (a1) around (a). (a) comprises a drug-containing composition (b1) and a water-swellable composition (b2), each occupying separate regions within (a). (b1) comprises drug (c), a swelling agent, and a drug-entraining agent (c1). (a1) is water-permeable, water-insoluble or comprises at least one delivery port.

DETAILED DESCRIPTION - A controlled release dosage form comprises a core (a) and a coating (a1) around (a). (a) comprises a drug-containing composition (b1) and a water-swellable composition (b2), each occupying separate regions within (a). (b1) comprises drug (c), a swelling agent (3.5 ratio), and a drug-entraining agent (c1)

(comprising 15 wt.% of the drug containing composition). (a1) is water-permeable, water-insoluble or comprises at least one delivery port.

An INDEPENDENT CLAIM is included for treating a disorder comprising administering a drug in the dosage form to a mammal.

USE - To release a control dosage form of a drug.

ADVANTAGE - The dosage forms are capable of delivering greater amounts of drug to the desired environmental of use with greater efficiency using smaller amounts of swelling materials, and also results in lower amounts of residual drug than do conventional compositions. In addition, the compositions begin delivering drug to the environment of use more quickly than do conventional osmotic controlled release dosage forms e.g. at least 70 wt.% of the low-solubility drug is released to a use environment within about 12 hours after introduction to the use environment. Thus the compositions are also capable of higher drug loading compared with the conventional compositions. The dosage forms are capable of rapidly delivering a low-solubility drug without the coating failing due to rupture as a result of excessive pressure within the core when the dosage form is introduced into an environment of use. The dosage forms are also capable of delivering the low-solubility drug in a solubilized form.

TECH POLYMERS - Preferred Composition: (c1) (at least 15 wt.%) further comprises: a swelling agent having a swelling ratio of at least 3.5; a fluidizing agent (at least 10 wt.%) having a solubility of at least 30 mg/ml; a solubilizer; an ionic swelling agent (c2); a concentration-enhancing polymer. (b2) comprises the swelling agent and a tableting aid and has a swelling ratio of at least 3.5. The mass ratio of (b1) to (b2) is at least 1.5.

The drug-containing composition further comprises ionizable cellulosic polymers, non-ionizable cellulosic polymers and vinyl polymers, and copolymers with substituents selected from OH, alkylacyloxy, or cyclicamido.

Preferred Components: (a) has a strength of at least 3 Kp/cm2 following tableting and comprises a solubilizer. The amorphous dispersion is a solid dispersion of (c) in the concentration-enhancing polymer. The concentration-enhancing polymer is ionizable cellulosic polymer, non-ionizable cellulosic polymer or vinyl polymer and copolymer having substituents. (a1) has a water flux (40 - 70) of at least 1x103 g/cm2 hour and a durability of at least 1 Kp/cm2. The drug has a maximum solubility of 20 mg/ml in aqueous solution that has pH 1 - 8. (a1) is porous with a dry-state density of less than 0.9 times that of the same coating material in non porous form.

Preferred Method: (a1) is formed from a substantially homogenous solution comprising a solvent, a cellulosic polymer (hydrophilic cellulosic polymer), and a non-solvent.

ORGANIC CHEMISTRY - Preferred Components: The swelling is (c2), which is selected from sodium croscarmellose and sodium starch glycolate. The solubilizer is an organic acid in the presence of which the drug has enhanced solubility. The fluidizing agent is an organic acid or a sugar. The substituent is hydroxyl, alkylcycloxy or cyclicamido.

ABEX EXAMPLE - A citrate salt of 1-(4-ethoxy-3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo(4,3-d)pyrimidin-5-yl) phenylsulfonyl)-4-methylpiperazine for treatment of penile erectile disfunction (a) having a solubility of about 20 microg/ml at pH 6 (drug 1) (35 wt.%), XYLITAB 200 (xylitol) (30 wt.%), polyethylene oxide (29 wt.%) with an average molecular weight of 600000, and EXPLOTAB (sodium starch glycolate) (5 wt.%) were blended for 20 minutes. Then magnesium stearate was added to prepare a final drug -containing composition (A), which was re-blended for 4 minutes. - A water-swellable composition (B) was prepared by blending (wt.%) EXPLOTAB (74.5), PROSOLY 90 (tableting aid silicitied microcrystalline cellulose) (25) and magnesium stearate (0.5). Tablets cores were formed by placing (A) (400 mg) in a standard die and gently leveling with the press. Then (B) (100 mg) was placed in the die on top of (A). The core was then compressed to a hardness of 11 Kp to obtain bilayer tablet core. A coating was applied by Vector LDCS-20 (pan-coater). The coating solution contained CA 398-10 (citric acid), PEG 3350 (polyethylene glycol), water and acetone in a weight ratio of 7/3/5/85 wt.%. The flow rate of the inlet heated drying air of the coater was set at 40 ft/3 minute with the outlet temperature of 25degreesC, nitrogen at 25 psi was used. The pan rotation was set to 20 rotations per minute (rpm). The coated tablets were dried at 50degreesC. Five 900 mum diameter holes were then drilled in the coating on (A)-side to provide 5 delivery ports per tablet. To Stimulate in vivo drug dissolution, tablets were placed in a simulated gastric solution (900 ml) for 2 hours, then transferred to a simulated intestinal environment solution (6 mM KH2PO4, 64 mM KCl, 35 mM NaCl, pH 7.2 and 210 mOsm/kg) (900 ml). Both solutions were stirred at 50 rpm. A residual dissolution test was performed. Residual drug was analyzed by HPCL using a watery symmetry C with its isotope of 18-column. The mobile phase consisted of 0.05 M triethanolamine (pH 3)/methanol/acetonitrile in a volume ratio of 58/25/17. Drug concentration (A1) was calculated by comparing UV (ultraviolet) absorber at 290 nm to the absorbance of Drug 1 standards. The amount of the drug remaining in the tablet was subtracted from the total initial amount of drug in the tablet to obtain the amount of released at each time. The results were: wt.% of drug released at time (hours) of 2, 3, 8, 14 and 20 was 25, 46, 74, 94 and 98 respectively.

L174 ANSWER 23 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1999-561836 [47] WPIX
ED 20050705
DNC C1999-163767 [47]
TI Stable tablets which rapidly dissolve in the oral cavity, comprising drug, saccharide and amorphous saccharide
DC B07
IN KAJIYAMA A; MASUDA Y; MIZUMOTO T; NYSHADHAM J R; YANAGISAWA M
PA (SHAK-N) SHAKLEE CORP; (YAMA-C) YAMANOUCHI PHARM CO LTD; (YAMA-C) YAMANOUCHI PHARM TECHNOLOGIES INC; (YAMA-C) YAMANOUCHI PHARMA TECHNOLOGIES INC; (ASTE-C) ASTELLAS PHARMA INC
CYC 81
AB WO 1999047124 A1 UPAB: 20060115
NOVELTY - Tablets which rapidly dissolve in the oral cavity comprise drug, saccharide and amorphous saccharide, and are prepared by molding and drying under moistening.
USE - As tablets which rapidly dissolve in the oral cavity.
ADVANTAGE - During drying under moistening the amorphous saccharides are irreversibly converted into crystalline saccharides, making the tablets stable to moisture during storage. The tablets can be formed from a single type of saccharide using conventional granulators and tabletting machines, making production simple and inexpensive.
TECH ORGANIC CHEMISTRY - Preferred Process: The tablets are obtained by dissolving the drugs, saccharides and crystalline saccharides in a solvent (to covert the crystalline saccharide to amorphous saccharide), eliminating the solvent, drying, molding and then drying under moistening (preferably at 30-100% relative humidity and 15-50degreesC). The amount of saccharide to amorphous saccharide is less than 2 wt. %.
ABEX EXAMPLE - Mannitol (602 g) and lactose (602 g) were dissolved in an aqueous glucose solution (15 w/v %; 433 g). The aqueous solution (157 g) was granulated using a screw pressure of 2.5 kg/cm2 then 1.5 kg/m2 and the granules were dried. The granules were mixed with peppermint flavor (10 g), stearic acid (12 g) and magnesium stearate (10 g) and molded using a rotary press to give tablets of 540 mg. - The tablets were subjected to 35degreesC and 85% relative humidity for 20 minutes and then dried at 50degreesC for 15 minutes. The final tablets had a breaking stress of 9.1 kp and dissolved in the oral cavity in 17 seconds.

L174 ANSWER 24 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1999-095239 [08] WPIX
ED 20050704
DNC C1999-027985 [08]
TI Oral dosage form used to deliver mucosal-irritating active agents to

stomach - comprise active ingredient e.g. tetracycline antibiotic and is in oval form and is film coated

DC A96; B05; B07

IN BEKKER J; BEKKER P J; DANSEREAU J; DANSEREAU R J

PA (PROC-C) PROCTER & GAMBLE CO

CYC 83

AB WO 1998056360 A2 UPAB: 20060115

Oral dosage form delivered to the stomach comprising (a) an active ingredient comprising tetracycline antibiotics, iron compositions, quinidine, non-steroidal antiinflammatory drugs (NSAID), alprenolol, ascorbic acid, captopril, theophylline, zidovudine and/or bisphosphonates and (b) excipients. The dosage form is oval in form and film coated to facilitate rapid oesophageal transit and avoid irritation in the mouth, buccal cavity, pharynx and oesophagus. The dosage form is 0.23-0.85 inches in length, 0.11-0.4 inches in width and 0.075-0.3 inches in thickness. The dosage form is a modified oval or caplet shape. The dosage form is a compressed tablet comprising particles of active ingredient and excipients. The film coating is soluble at pH 1.2-5. The film coating preferably comprises hydroxypropylmethylcellulose, hydroxypropylcellulose, carboxymethylcellulose, methylcellulose, ethylcellulose, acrylic resins, polyvinylpyrrolidone and/or gelatine. The active ingredient comprises emperonium bromide, doxycycline, iron compositions, potassium chloride, quinidine, non-steroidal antiinflammatory drug, alprenolol, ascorbic acid, captopril, theophylline, zidovoudine, risedronate, alendronate and/or pamidronate (preferred). The dosage form comprises 0.25-40% risedronate. The particles of active ingredients are film coated.

USE - The dosage form is used to deliver active ingredients to the stomach. The dosage form is used for treating diseases characterised by abnormal calcium or phosphate metabolism and is particularly useful for administration of active ingredients that may cause patient complaints such as heartburn, oesophageal burning, pain and/or difficulty upon swallowing and/or pain existing behind and/or mid-sternum such as those agents with pH < 2-3, drugs with cytotoxic activity (caustic) and/or those that cause the local development of a hyperosmolar solution that causes mucosal desiccation.

ADVANTAGE - The oval form and film coating facilitate rapid oesophageal transit and avoid irritation in the mouth, buccal cavity, pharynx and oesophagus which improves upper gastrointestinal tract safety. The dosage form protects the epithelial and mucosal tissue of the mouth, buccal cavity, pharynx and oesophagus from erosion, ulceration or other irritation suffered by direct contact of these tissues with the active ingredient. ABDT WO1998056360

Oral dosage form delivered to the stomach comprises:

(a) an active ingredient comprising tetracycline antibiotics, iron compositions, quinidine, non-steroidal antiinflammatory drugs

(NSAID), alprenolol, ascorbic acid, captopril, theophylline, zidovudine and/or bisphosphonates and
(b) excipients.
The dosage form is oval in form and film coated to facilitate rapid oesophageal transit and avoid irritation in the mouth, buccal cavity, pharynx and oesophagus.
USE
The dosage form is used to deliver active ingredients to the stomach. The dosage form is used for treating diseases characterised by abnormal calcium or phosphate metabolism and is particularly useful for administration of active ingredients that may cause patient complaints such as heartburn, oesophageal burning, pain and/or difficulty upon swallowing and/or pain existing behind and/or mid-sternum such as those agents with pH < 2-3, drugs with cytotoxic activity (caustic) and/or those that cause the local development of a hyperosmolar solution that causes mucosal desiccation.
The dosage of risedronate is 1-40 (1-30) mg/day orally.
ADVANTAGE
The oval form and film coating facilitate rapid oesophageal transit and avoid irritation in the mouth, buccal cavity, pharynx and oesophagus which improves upper gastrointestinal tract safety. The dosage form protects the epithelial and mucosal tissue of the mouth, buccal cavity, pharynx and oesophagus from erosion, ulceration or other irritation suffered by direct contact of these tissues with the active ingredient.
EXAMPLE
Film-coated, oval risedronate tablets were prepared by making granules containing risedronate, coating the granules, compressing into a tablet and film-coating the tablets.
The granulation was prepared by dissolving PVP (10 kg) in purified water (75 kg). Risedronate sodium (2.5 kg), anhydrous lactose (100 kg) and microcrystalline cellulose (100 kg) were mixed in a high-shear mixer for 3 minutes. The mixture was granulated with the PVP solution with mixing over 5 minutes. The wetted mass was dried in a fluid-bed drier at an inlet temperature of 60°C. The dried material was milled using a hammer mill to achieve the desired granule size. The granulation was then coated and compressed into tablets by dissolving hydroxypropylmethylcellulose E-15 (5 kg) in purified water (50 kg) at 60°C with continuous mixing. The mixture was cooled to 30°C and mixed until dissolved.
The risedronate sodium granules (106.8 kg) were added to a coating column. The hydroxypropylmethylcellulose E-15 solution was sprayed on at an inlet temperature of 50°C. After coating, the granules were dried at an inlet temperature of 60°C. The coated granules were transferred to a twin-shell blender and crospovidone (3 kg) and microcrystalline cellulose (15 kg) were added and mixed for 5 minutes. Magnesium stearate (0.5 kg) was added

and the mixture mixed for 3 minutes before compressing into tablets on a rotary press.
Film-coating suspension was prepared by adding hydroxypropylmethylcellulose E-5 (2.3 kg) to part of purified water at 80°C with agitation. The remaining purified water (to 50 kg) was added at 10°C and the mixture mixed until dissolved. Polyethylene glycol 6000 (PEG 6000; 0.92 kg) was added to purified water with mixing. 'FD&C Blue #1 Lake' (RTM) (0.05 kg) and silicon dioxide (0.05 kg) were added to the PEG 6000 solution and dispersed using a high-shear mixer for 10-25 minutes. This pigment suspension was added to the polymer solution and mixed. Core tablets (2.5 mg each; 120 kg) were loaded into a 48-inch, side-vented, coating pan. The tablets were preheated until the exhaust temperature reached 40°C and spraying was begun. The coating suspension was applied using an inlet air temperature of 40°C at 250 g/minute. The tablets were then cooled and discharged. (TF)
PREFERRED PRODUCT
The dosage form is 0.23-0.85 inches in length, 0.11-0.4 inches in width and 0.075-0.3 inches in thickness. The dosage form is a modified oval or caplet shape. The dosage form is a compressed tablet comprising particles of active ingredient and excipients. The film coating is soluble at pH 1.2-5. The film coating comprises hydroxypropylmethylcellulose, hydroxypropylcellulose, carboxymethylcellulose, methylcellulose, ethylcellulose, acrylic resins, polyvinylpyrrolidone and/or gelatine.
The active ingredient comprises emperonium bromide, doxycycline, iron compositions, potassium chloride, quinidine, non-steroidal antiinflammatory drug, alprenolol, ascorbic acid, captopril, theophylline, zidovoudine, risedronate, alendronate and/or pamidronate (preferred). The dosage form comprises 0.25-40% risedronate.
The particles of active ingredients are film coated.

L174 ANSWER 25 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1997-350190 [32] WPIX Full-text
ED 20050518
CR 1992-284351; 1998-609219
DNC C1997-113009 [32]
TI Solid dosage forms containing microcrystalline cellulose - used for delivery of agrochemicals, pharmaceuticals and veterinary products
DC A97; B07; C04; C07; J04
IN FLECK E G; IBRAHIM N I; MEHRA D K
PA (FMCC-C) FMC CORP
CYC 1
PI US 5643591 A 19970701 (199732)* EN 6[0]
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ADT US 5643591 A CIP of US 1991-642099 19910116; US 5643591 A CIP of US 1991-814186 19911219; US 5643591 A US 1994-230407 19940420

PRAI US 1994-230407 19940420
US 1991-642099 19910116
US 1991-814186 19911219

IPCR A01N0025-10 [I,A]; A01N0025-10 [I,C]; A01N0025-34 [I,A]; A01N0025-34 [I,C]; A61K0009-16 [I,A]; A61K0009-16 [I,C]

EPC A01N0025-10; A01N0025-34; A61K0009-16H4; A61K0009-16H6F

NCL NCLM 424/408.000
NCLS 424/409.000; 424/464.000; 424/465.000

AB US 5643591 A UPAB: 20050827
Solid dosage form comprises compacted particulate blend comprising: (a) compression mouldable finely divided homogeneous particulate mixture of 0.05-25 % microcrystalline cellulose of particle size 20-90 μ and a nitrogen compound comprising urea, ammonium sulphate or ammonium phosphate, in a weight ratio of 10:1 - 1:10; (b) 16-65 % active material compatible with (a) comprising herbicides, plant growth regulators and/or pesticides; and (c) 0-29 % additive comprising glidants, lubricants, dispersants, surfactants and/or auxiliary disintegrants.

USE - The dosage forms are useful in agricultural and veterinary products pharmaceuticals, animal and human foods, swimming pool additives, industrial biocides for oil wells and other applications, cosmetics, household pesticides and dye manufacturing, particularly in the agricultural field as herbicides, plant growth regulators and biocides of all types such as pesticides, especially atrazine, benazone, trifluralin, propanil, metribuzin, alachlor, butachlor, bromoxynil, clomazone, oxadiazon, lorsban, bifenox, aldicarb, monocrotophos, propoxur, diflubenzuron, carbofuran, permethrin, carbaryl, cypermethrin, endosulfan, cyfluthrin, bifenthrin, terbufos, fenamiphos, cadusafos, paclobutrazol, glyphosine and giberellic acid.

ADVANTAGE - The composition can be compacted to form shaped, solid dosage forms such as tablets which disintegrate rapidly in aqueous media. MCC is a low cost excipient for producing compacted solid dosage forms. The tablets can be bisected or multisected so that they can be divided by hand or machine for delivery of fractional amounts of active ingredient. he compositions have improved properties including rapid disintegration and no diminution of properties attributable to the MCC. Rapid disintegration even at low temperatures (such as the dew point in agrochemical environments) reduces avian toxicity when the active agent is a type which would present risk if broadcast in slow disintegrating granules or extrudate form. The carrying capacity of the particulate blend is very high, as much as 65 wt% thus enhancing the cost effectiveness.

ABDT US5643591
Solid dosage form comprises compacted particulate blend comprising:

(a) compression mouldable finely divided homogeneous particulate mixture of 0.05-25 % microcrystalline cellulose of particle size 20-90 μm and a nitrogen compound comprising urea, ammonium sulphate or ammonium phosphate, in a weight ratio of 10:1 - 1:10; (b) 16-65 % active material compatible with (a) comprising herbicides, plant growth regulators and/or pesticides; and (c) 0-29 % additive comprising glidants, lubricants, dispersants, surfactants and/or auxiliary disintegrants.

USE

The dosage forms are useful in agricultural and veterinary products pharmaceuticals, animal and human foods, swimming pool additives, industrial biocides for oil wells and other applications, cosmetics, household pesticides and dye manufacturing, particularly in the agricultural field as herbicides, plant growth regulators and biocides of all types such as pesticides, especially atrazine, benazone, trifluralin, propanil, metribuzin, alachlor, butachlor, bromoxynil, clomazone, oxadiazon, lorsban, bifenox, aldicarb, monocrotophos, propoxur, diflubenzuron, carbofuran, permethrin, carbaryl, cypermethrin, endosulfan, cyfluthrin, bifenthrin, terbufos, fenamiphos, cadusafos, paclobutrazol, glyphosine and giberellic acid.

ADVANTAGE

The composition can be compacted to form shaped, solid dosage forms such as tablets which disintegrate rapidly in aqueous media. MCC is a low cost excipient for producing compacted solid dosage forms. The tablets can be bisected or multisected so that they can be divided by hand or machine for delivery of fractional amounts of active ingredient.

The compositions have improved properties including rapid disintegration and no diminution of properties attributable to the MCC. Rapid disintegration even at low temperatures (such as the dew point in agrochemical environments) reduces avian toxicity when the active agent is a type which would present risk if broadcast in slow disintegrating granules or extrudate form.

The carrying capacity of the particulate blend is very high, as much as 65 wt% thus enhancing the cost effectiveness.

EXAMPLE

'Avicel PH 105' (RTM; MCC, 20 μm average particle size, FMC corporation) and urea granules (milled to 20-60 USS mesh) were dry blended in a PK mixer to form blends of MCC/urea wt ratio 100/0, 66.6/33.4, 50/50, 25/75 and 0/100. The thickness of the tablets were 6.44, 7.32, 6.82, 6.41 and 6.32 mm and the disintegration time, determined by immersing each tablet in 400 ml water at room temperature was 240, 90, 15, 30 and no disintegration respectively. (JM)

PREFERRED COMPOSITION

The ratio of microcrystalline cellulose to urea is 2:1 - 1:3 Where

the nitrogen compound is urea the active agent is an agricultural chemical preferably a herbicide o pesticide.
Especially the composition comprises 0.05-2.5 wt% (based on MCC) of a suspending agent for MCC comprising water soluble hydrocolloids compatible with ad effective for assisting hydration of MCC, particularly sodium carboxymethyl cellulose.

L174 ANSWER 26 OF 28 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
AN 1996-188091 [19] WPIX Full-text
ED 20050511
CR 1996-188094; 1999-033979
DNC C1996-060013 [19]
TI Loading biologically active solute into crosslinked gel - in presence of loading polymer and pref. salt, to increase loading and stabilise active cpd., used e.g. in drug delivery
DC A96; A97; B07; C07; D25; P32
IN GEHRKE S H; LORELLE U; LUPTON E C; SCHILLER M E; UHDEN L; VAID N
PA (UYCI-N) UNIV CINCINNATI
CYC 24
PI WO 9602239 A2 19960201 (199619)* EN 62[1]
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AU 9532752 A 19960216 (199622) EN
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US 5603955 A 19970218 (199713) EN 19[1]
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WO 9602239 A3 19970213 (199722) EN
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US 5674521 A 19971007 (199746) EN 20[1]
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ADT US 5603955 A US 1994-276462 19940718; US 5674521 A Div Ex US 1994-276462 19940718; US 5674521 A US 1995-425275 19950420; AU 9532752 A AU 1995-32752 19950718; WO 9602239 A3 WO 1995-US9838 19950718
FDT US 5674521 A Div ex US 5603955 A; AU 9532752 A Based on WO 9602239 A
PRAI US 1994-276462 19940718
IPCR A61K0009-20 [I,A]; A61K0009-20 [I,C]; A61K0009-22 [I,A]; A61K0009-22 [I,C]; A61L0015-16 [I,C]; A61L0015-60 [I,A]
EPC A61K0009-20H6F; A61K0009-20H6F2; A61K0009-20P; A61L0015-60
NCL NCLM 424/484.000
NCLS 424/486.000; 424/487.000; 424/488.000; 514/944.000; 516/102.000; 516/104.000; 516/105.000; 516/106.000; 516/107.000
AB WO 1996002239 A2 UPAB: 20060110
A method of loading a solute (I) into a crosslinked polymer gel (CPG) network involves contacting a CPG which contains a solvent with a soln. contg. (I) and a loading polymer (LP) (which is pref. soluble in the same solvent as CPG), under conditions such that the solute is

selectively partitioned into CPG and for (I) to retain activity while in the network.

Also claimed are: (a) a method for delivering a biologically active (I) into an environment of use, by partitioning (I) into a responsive gel as above, then allowing expansion or collapse of the gel under conditions which release (I); (b) a novel 3-dimensional, responsive polymer gel network, comprising a CPG, a protectant (II) and a biologically active (I); (c) a delivery system comprising a polymer gel network including (I) to be delivered, a salt (ST) and LP, where ST and/or LP reduce loss of activity of (I) while within the gel; (d) a method of maintaining activity of a biologically active (I) in a CPG, by contacting a soln. of (I) and a (II) soln. contg. LP and ST with CPG under conditions such that (I) and (II) are introduced and selectively partitioned into CPG while maintaining activity of (I) during and after partitioning; and (e) a gel as in (b) loaded with at least 10 wt.% of a high mol. wt. (I).

USE - The loaded CPG networks are useful for controlled delivery of drugs (I), e.g. as oral dosage forms (such as tablets), injectable microspheres or reservoirs of transdermal devices. Release of (I) may be in response to temp. or pH (e.g. body temp. or intestinal pH), or by simple passive diffusion. Numerous specific drugs (both as therapeutic categories and individual cpds.) are listed in the disclosure. - The networks may also be used in a wound dressing (to release medicament into the wound), an iontophoretic drug delivery system (which delivers drug when exposed to a current) or a controlled release device for pest control agents, cleaning agents (specifically an enzyme, detergent or bleach) or (more generally) agents to be delivered into organic solvents (all claimed). - (I) is specifically a protein (pref. an enzyme), polypeptide, nucleoprotein, glycoprotein or lipoprotein (all claimed), and pref. has mol. wt. at least 1000. - Release of (I) is specifically in response to a change in the environmental conditions to which CPG is exposed, esp. a change in temp., electrical field, photon energy, pH, solvent compsn., ion concn., (I) concn. or pressure.

ADVANTAGE - High (I) loadings in CPG (i.e. up to 40 wt.% (I) base on CPG) are obtd. and/or inactivation/denaturation of (I) during and after loading is prevented. Both of these features can be achieved in a single step, and can work synergistically. ABDT WO9602239

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EXAMPLE

A soln. of 1g dextran (mol. wt. 39100) in 10 ml 0.02M aq. NaOH was treated dropwise with divinyl sulphone (0.12g/g dextran) and moulded for 24 hrs. to give gel cylinders. After washing free of unreacted reagents, the cylinders were equilibrated with 3ml of soln. contg. 12 wt. % PEG (mol. wt. 10000), 0.22M KCl and 1 mg/ml amylase.

Loading of the gel was 9.2 wt.%, about half being amylase and the other half protectant (i.e. KCl and PEG). Activity retention of the amylase was almost 100%. (RMH)

PREFERRED MATERIALS

CPG is obtainable from one of a gp. of water-soluble polymeric precursor materials which separate into two or more aq. phases when combined with another polymer of the gp.

The precursor is pref. selected from polyethylene oxide, polyethylene glycol, PVA, methylcellulose, dextran, hydroxypropyl dextran, ethyl-hydroxyethyl cellulose, PVP, hydroxypropyl cellulose, hydroxypropyl starch, polypropylene glycol, polysucrose, CMC, carboxymethyl dextran, dextran sulphate and methoxypolyethylene glycol.

Alternatively CPG is a modified food starch gel or a cellulose ether gel.

CPG, (I) and LP are contacted in presence of ST, to enhance partitioning of (I) into CPG. (II) is LP (pref. a soln. of polyethylene glycol) or ST.

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AN 1994-157526 [19] WPIX Full-text
ED 20050507
DNC C1994-072444 [19]
DNN N1994-123753 [19]
TI Rotary tablet press - has hydrocylinder with journal bearings and punches operated by levers whose axles lie at a formula defined distance from the bearings
DC B07; J04; P71
IN SMIRNOV A G
PA (TECH-R) TECHN EQUIP SUPPLY CONS INST
CYC 1
PI SU 1798199 A1 19930228 (199419)* RU 3[2]
<--
ADT SU 1798199 A1 SU 1988-4604998 19880810
PRAI SU 1988-4604998 19880810
IPCR B30B0011-02 [I,C]; B30B0011-08 [I,A]
AB SU 1798199 A1 UPAB: 20050507
Press comprises bed (1), rotor (2) on whose periphery are mounted upper (3) and lower (4) punches and dies (5), cams (6) for upper (3), and (7) for lower (4) punches, hopper (8), and a reciprocating drive for moving the punches which includes lower (9) and upper (10) pressure application rollers. The roller (1) can rotate in two clamping levers (11) which are hinged on their left to vertical member (12) mounted on bed (1). The lower roller (9) is attached to clamping levers (13).

The levers are linked to a hydrocylinder piston via a journal bearing whose position takes account of the coefft. of thermal expansion of

the body elements. This ensures that even pressure is maintained during temp. change in the circulating fluid.

USE - Used in pharmaceutical, chemical and other inds. to produce tablets.

ADVANTAGE - Quality of tablets is improved since it is ensured that they are of constant mass.

FS CPI; GMPI

MC CPI: B11-C05; B12-M11B; J04-A05

CMC UPB 20050507

M6 *01* Q435 R038 R112 R150 M903